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Research Education Practice

Letter:

About the Special Kidney Issue

Integrating Point of Care Ultrasound into Nephrology Fellowship Training: Insights from a Pilot Program

Nephrology Fellowship Clinician-Performed Ultrasound Curriculum

Case File:

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POCUS Allows for Rapid Elucidation of Acute Kidney Injury in a Patient with Progressive Multiple Myeloma

Case Report:

Recovery of Severe Acute Kidney Injury in a Patient with COVID-19: Role of Lung Ultrasonography

Incidentalomas Among Healthy Nephrology Fellow Volunteers at POCUS Workshops: A Case Series

Point of Care Ultrasound in Monitoring of Post-Renal Biopsy Bleeding

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Point of Care Ultrasound of the Hemodialysis Vascular Access

Special Kidney Issue

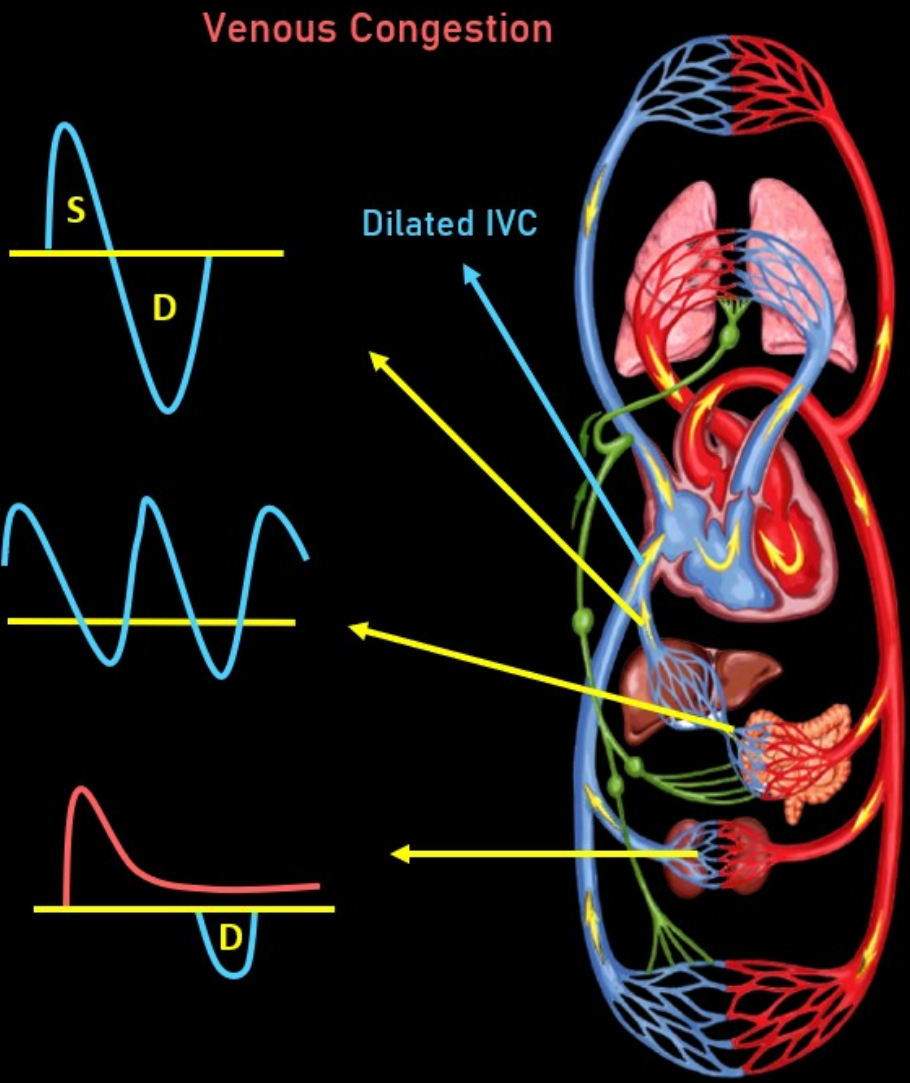

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Table of Contents | Volume 7 | Kidney Issue | February 2022

Letter

3-4 **About the Special Kidney Issue**
Abhilash Kortala, MD; Nathaniel Reisinger, MD

5-6 **Integrating Point of Care Ultrasound into Nephrology Fellowship Training: Insights from a Pilot Program**
Ann Young, MD PhD; Benoit Imbeault, MD; Alberto Goffi, MD; Alireza Zahirieh, MD; Claire Kennedy, MD; Daniel Blum, MDCM; Ron Wald, MDCM MPH; William Beaubien-Souligny, MD PhD

7-8 **Nephrology Fellowship Clinician-Performed Ultrasound Curriculum**
Nathaniel Reisinger, MD; Nova Panebianco, MD, MPH

Case File

9-10 **Point of Care Ultrasound Diagnosis of Pseudoaneurysm of an Upper Extremity Arteriovenous Dialysis Graft**
Forrest Lindsay-McGinn, MD; Nathaniel C. Reisinger, MD

11-13 **Utility of Nephrologist-Performed Point of Care Ultrasonography in the Evaluation of Hyponatremia**
Mahmud Saqib, MD; Gregory Capelli, DO; Abhilash Koratala, MD

14-16 **Point of Care Ultrasonography to Monitor Decongestive Therapy in Heart Failure: Seeing is Believing**
Abhilash Koratala, MD

17-20 **Evaluation of Venous Congestion Using Beside Ultrasonography by the Nephrology Consultant: The VExUS Nexus**
Abhilash Koratala, MD

21-23 **Massive Lymphocele Associated with Allograft Hydronephrosis: An Ultrasound Case Study**
Harini Bejjanki, MD; Kawther F. Alquadan, MD; Abhilash Koratala, MD

24-26 **POCUS Allows for Rapid Elucidation of Acute Kidney Injury in a Patient with Progressive Multiple Myeloma**
Liann Abu Salman, MD; Nathaniel Reisinger, MD

Case Report

27-29 **Recovery of Severe Acute Kidney Injury in a Patient with COVID-19: Role of Lung Ultrasonography**
Varun Madireddy, MD; Daniel W. Ross, MD MPH; Deepa A. Malieckal, MD; Shamir Hasan, DO; Azzour Hazzan, MD; Hitesh H. Shah, MD

30-32 **Incidentalomas Among Healthy Nephrology Fellow Volunteers at POCUS Workshops: A Case Series**
Ira Blau, MD; Behdad Besharatian, MD; Nathaniel Reisinger, MD

33-34 **Point of Care Ultrasound in Monitoring of Post-Renal Biopsy Bleeding**
Natalie N. McCall, MD; Anna Burgner, MD, MEHP

Table of Contents (con't)

Review

35-44 **Ultrasonography in Acute Kidney Injury**
Andrew A. Moses, MD MA; Hilda E. Fernandez, MD

45-50 **Focused Cardiac Assessment in Kidney Care**
Vineet Veitla, MD; Bhavna Bhasin, MD

51-58 **POCUS in Intensive Care Nephrology**
Randi Connor-Schuler, MD; Jonathan Suarez, MD

59-64 **Role of Point of Care Ultrasonography in Patients with COVID-19 Associated Acute Kidney Injury**
Daniel W. Ross, MD; Zubair Hasan, MD

65-77 **Integrative Volume Status Assessment**
David Kearney, MD; Nathaniel Reisinger, MD; Sadichhya Lohani, MBBS

78-87 **Machine Learning in Point of Care Ultrasound**
Momodou L. Sonko, BS; T. Campbell Arnold, BS; Ivan A. Kuznetsov, BS

88-93 **Nuts and Bolts of a POCUN Program**
Noelle M. Northcutt, MD; Nathaniel C. Reisinger, MD

94-104 **Bedside Assessment of the Kidneys and Bladder Using Point of Care Ultrasound**
Patrick J. Taus, MD, PhD; Surya Manivannan, MD; Ria Dancel, MD

105-109 **Point of Care Ultrasound of the Hemodialysis Vascular Access**
Larissa Kruger Gomes, MD; Het Patel, MD; Nikhil Agrawal, MD; Yael Vin, MD

Letter

About the Special Kidney Issue

We know what you're thinking. we've heard it a thousand times: "Oh, you're a kidney doctor who dinks around with ultrasound? What do you look for? Hydronephrosis?" You may be asking, "Is this issue just going to be a bunch of pictures of hydronephrosis and distended bladders?" And yes, for the thousandth time, in acute kidney injury it's almost never wrong to get a kidney and bladder ultrasound as part of the initial workup.

But there's so much more! Point of care ultrasound is an incredibly valuable tool to the nephrologist, not just for quickly assessing for urinary outflow obstruction, but for overall assessment of physiology, particularly for volume status assessment. Our *raison d'être* is building the evidence for point of care ultrasound in nephrology and to that end we present for your approval The POCUS Journal: Kidney Edition.

As nephrologists, we see consults across an incredible range of clinical settings from the cardiac surgery ICU to the home dialysis clinic and from the glomerulonephritis clinic to the liquid oncology ward. Our scope of practice is likewise broad. We are consulted on electrolyte disorders, acid-base issues, mineral metabolism concerns, and hypertension but we also see patients with acute kidney injury and chronic kidney disease as well as any patient needing dialysis including intermittent, continuous, and peritoneal. We are primary care providers for those with CKD and critical care physicians for those needing CRRT.

In all of these patients: those with hypertension, hyponatremia, metabolic alkalosis, acute kidney injury, chronic kidney disease, and dialysis dependence we are constantly asking: what is the volume status? Will the patient improve with diuretics in the cardiorenal syndrome? Will this hypovolemic patient with AKI respond to a crystalloid bolus? How much ultrafiltration do I prescribe for this routine hemodialysis session? As you will read in the ensuing pages, point of care ultrasound helps answer these questions.

Moreover, we are most often consulted in situations where the kidney problem is not the overarching concern, but rather the first end-organ manifestation of a potentially life-threatening or emergent systemic problem. Sometimes this is obvious like in a patient rigoring with septic shock with a lactate of 10 on his way to the MICU or the patient who spent 4 hours on cardiopulmonary bypass with a prolonged aortic crossclamp time following

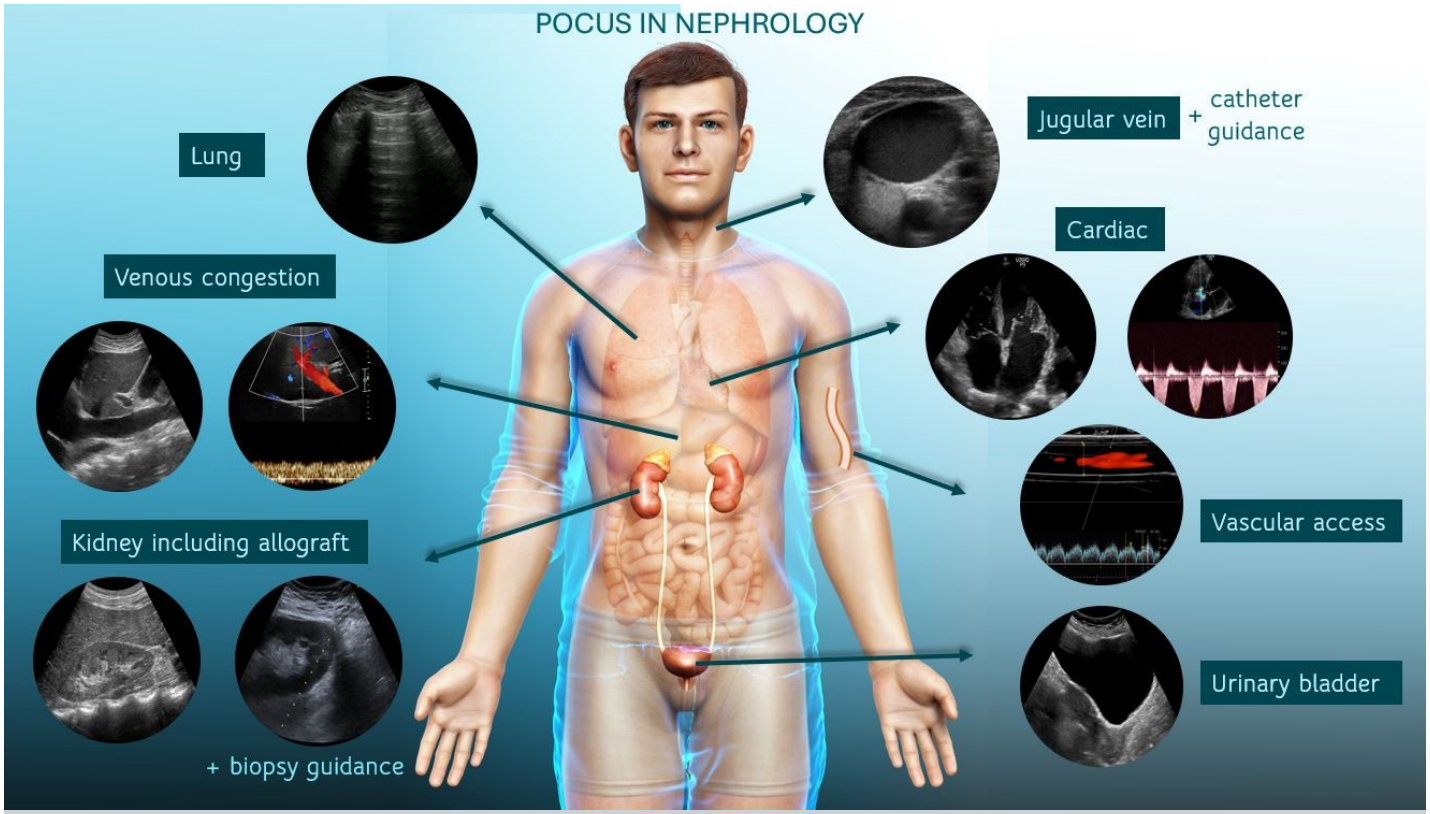

Figure 1. POCUS in Nephrology.

a complex cardiac surgery. Other times, the cause of the fall in GFR is cryptic and transient or subtle like a hemodynamic rise in creatinine in a patient on combination of RAAS blockers, diuretics, and NSAIDs or a patient with mild tubular injury due to failure of autoregulation related to transient hypotension during induction anesthesia.

One of our first experiences with point of care ultrasound is illustrative. A 45-year-old man with heart failure and a reduced ejection fraction due to non-ischemic cardiomyopathy was admitted for heart failure optimization in the coronary care unit. He had had a pacemaker placed on Friday and transferred to the CCU on Monday with acute kidney injury with creatinine rising from 1 to 3 over the weekend. Our signout noted his blood pressures were “soft” and his physical exam was “difficult.” Nephrology had been consulted over the weekend and proposed workup with urinalysis and kidney ultrasound was pending. Our physical exam was indeed challenging. His jugular veins were obscured due to his body habitus and his heart sounds were muffled. He was altered and could not hold his breath to assess for pulsus paradoxus. Ultimately our team performed a bedside echocardiogram which revealed a large pericardial effusion and tamponade physiology. He went to the OR within hours for a pericardial window and had 1 liter of blood drained with resolution of the hypotension and acute kidney injury post-operatively—having had cardiac tamponade complicating pacemaker placement.

In retrospect what strikes me most about this case—apart from the excellent demonstration of the utility of POCUS—is the proximity of the nephrologist to the front line of care in emergent situations. A nephrologist equipped with POCUS would have made the diagnosis 48 hours earlier, avoiding potential lasting harm by mitigating the extent of organ injury. Our experience as practicing nephrologists is exactly that: POCUS expedites care and adds value, not just for routine matters of exclusion of urinary obstruction, but overall integrative patient assessment.

We planned and executed this issue of The POCUS Journal as an entry point for nephrologists interested in getting started with point of care ultrasound and for providers from other disciplines to get a sense of what it’s like to be a nephrologist and gain some perspective on cases we see. For this issue, we are delighted to collaborate with the Renal Fellow Network—an online community of free open-access online medical education geared toward nephrology fellows. We will be publishing blog post commentaries simultaneously with the release of this issue to broaden our impact and reach more trainees.

In this issue, you’ll find a panoply of articles on point of care ultrasound in nephrology. We start with two original research pieces on educating the next generation of nephrologists. We move on to case files and reports ranging from the mundane—an unusual case of unexpected obstructive nephropathy—to the sublime—integrating focused cardiac ultrasound and venous excess ultrasound into our daily rounds. We wrap up with reviews on a diverse range of topics including established topics like kidney ultrasound, but also practice-changing POCUS breakthroughs such as quantitative lung ultrasound and VExUS.

Finally, we’d like to thank the huge community of nephrologist- and non-nephrologist-POCUS enthusiasts who contributed to this issue. First we’d like to thank all of our outstanding fellows who submitted excellent cases. We’d like to thank all of our authors and reviewers who volunteered, taking the time out of their busy lives We’d especially like to thank editor-in-chief Jamie Galen and former editor-in-chief Amer Johri for trusting us with this amazing opportunity, surrendering their journal to subspecialists for a month. Finally, we would be remiss if we did not thank managing editor Julia Herr. Without her organization, diligence, and hard work this issue could not have happened.

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Letter

Integrating Point of Care Ultrasound into Nephrology Fellowship Training: Insights from a Pilot Program

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In nephrology, point of care ultrasound (POCUS) has multiple applications including the rapid evaluation of acute kidney injury, enhancing the initial evaluation of chronic kidney disease, direct evaluation of vascular access, and improved fluid balance management in acute and chronic settings [1, 2]. Recently, the role of POCUS has been formally acknowledged by the *American College of Physicians* and curricula specific to nephrology have been proposed [3, 4]. However, the integration of a novel clinical skill into a field comes with its unique set of challenges. Above all, most nephrologists in leadership roles within fellowship training programs lack POCUS experience, which represents a significant barrier for adequate exposure and teaching. Although educational curricula centered on nephrology have been proposed, the optimal model to ensure adequate POCUS exposure considering the scarcity of expertise among educators is not known.

In 2018, we aimed to develop a pilot POCUS program for nephrology fellows at the University of Toronto. The focus was limited to renal POCUS with the aim of enabling the operator to detect hydronephrosis and to evaluate chronic kidney disease by measuring longitudinal kidney length. The objective was to provide adequate POCUS exposure without a dedicated POCUS rotation. During phase 1, the trainees were given a brief document demonstrating optimal transducer position for kidney assessment, kidney measurements, examples of hydronephrosis and renal atrophy. Two weeks later, a two-hour hands-on POCUS session was held. Six stations were organized with experienced instructors and volunteer models including healthy individuals and patients with renal anomalies including hydronephrosis and renal atrophy. Instructors included four nephrologists, one intensivist and one ultrasound technician with experience ranging from 1 to 15 years. Trainees had the opportunity to rotate between stations to benefit from various experience and teaching styles.

For phase 2, resources for self-directed learning were organized at two hospitals. These included access to dedicated POCUS devices and the presence of one supervisor per site able to provide ad hoc assistance if needed. We proposed to fellows undergoing their clinical rotations the goal of autonomously performing three or more renal POCUS assessments per week for the following four month period, aiming for a total of 50 studies. During their clinical rotations, nephrology fellows are usually involved in the care of inpatients and ambulatory patients including patients with end-stage kidney disease undergoing maintenance dialysis. They were asked to keep a log to determine how many assessments were performed and were also encouraged to digitally record their assessment for retrospective feedback.

Twenty trainees participated in phase 1. The trainees were generally satisfied with the training session as an introduction to POCUS. Participants emphasized the benefit of having models comprised of both healthy volunteers and volunteers with renal pathologies. Phase 2 of the pilot program was initiated two months after the hands-on training session. The delays were due to obtaining dedicated ultrasound equipment to each site. Fifteen trainees were in clinical rotations during this period. During the first month, it became apparent that the dedicated US devices were underused. The US device was used autonomously 11 times (out of 100 total expected uses) within the first month of phase 2. Furthermore, almost all exams were performed under direct supervision of the local POCUS supervisor. To improve the use of the US device and to stimulate interest, reminders accompanied with ultrasound images and tips were sent to the fellows during the second month

of phase 2. However, the US device remained underused during this period. After the second month, phase 2 was interrupted.

This is the first report describing the implementation of a pilot POCUS training program for nephrology fellows in a Canadian institution. The program was based on a structured training session followed by self-directed learning during clinical rotations. The main objective was to provide adequate exposure in an environment where POCUS expertise is scarce. Unfortunately, the program failed to provide adequate exposure to POCUS for nephrology fellows. Despite the success of phase 1, on-site dedicated US devices were underutilized in phase 2 of the project.

Formal POCUS training is not currently part of the nephrology core curriculum in Canadian institutions. We observed a definitive interest among nephrology fellows to integrate POCUS into their training. An effective training model would require giving basic POCUS training followed by direct hands-on experience. The best method for the latter would be direct supervision by front-line clinicians during clinical rotations [5], although this would require supervisors to be trained in POCUS which represent a significant barrier.

Ensuring adequate POCUS exposure could be achieved through a dedicated ultrasound rotation with an experienced trainer [3]. However, learning to integrate POCUS into the clinical decision-making process is an important skill that may be neglected if POCUS is done separately from clinical work. Another solution would be to favor a self-directed learning approach during clinical rotations with rapid access to a local POCUS expert to offer ad hoc supervision and feedback. This approach would have the potential advantage of requiring only a few local POCUS experts while ensuring adequate exposure integrated to clinical work for the fellows in training. However, our experience questions the feasibility of this type of approach.

In summary, this pilot POCUS program based on self-directed learning during clinical rotations was insufficient to provide nephrology trainees with adequate POCUS exposure during fellowship training. However, we identified a strong interest in POCUS among nephrology fellows. During this pilot program, we identified 3 essential components that were missing to ensure adequate exposure to POCUS within the nephrology curriculum: 1) direct supervision, 2) adequate time, and 3) program endorsement of POCUS as an official training objective. Future efforts should focus on providing these essential components to build an effective POCUS program.

Acknowledgements

We want to thank Bonnie Cheng RDMS, CMRTO, B.Ed., sonographer and clinical application specialist at FUJIFilm Sonosite, for offering her time as an instructor for the POCUS workshop and well as Michael Taranovsky, Territory Manager at FUJIFilm Sonosite, who provided ultrasound devices during phase 1 and phase 2 of this pilot program. William Beaubien-Souligny is supported be Fonds de recherche du Québec en Santé.

Statement of Ethics

This is a program report and does not constitute research. No identifiable or sensitive personal information was collected or reported. As such, Research Ethics Board approval was not necessary for the publication of this report.

Disclosures

The authors report no financial or other competing interests associated with the present report.

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Nephrology Fellowship Clinician-Performed Ultrasound Curriculum

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Introduction

Fluid overload (FO) contributes significantly to the development of cardiovascular disease among patients with end-stage kidney disease (ESKD) on hemodialysis (HD), yet remains underappreciated due to limitations of the physical exam [1]. Lung ultrasound (US) is an established tool for quantification of FO [2]. Previous validation of quantitative lung US among nephrology attendings using a remote web-based lung ultrasound training has been demonstrated [3]. Interest in ultrasound education among nephrology fellows is high [4]. Clinician-performed ultrasound curricula for nephrology fellows have been described previously, however fellows' competency in quantitative lung US has not been described [5]. In the present study we aimed to assess the current level of knowledge among nephrology fellows as well as the efficacy of a brief training course in quantitative lung US.

Methods

For lung ultrasound didactics we employed a web-based, mobile-optimized, app-supported curriculum covering the basics of lung US as well as quantitative lung US. Pre- and post-course short-answer didactic content tests were used to assess learning. Pre- and post-course surveys using a 5-point Likert scale assessed confidence in five domains of clinician-performed ultrasound including psychomotor skills, knobology, image acquisition, lung US image interpretation, and clinical integration.

Additionally, trainees had a single 15-minute hands-on, one-on-one teaching session with a peer experienced in clinician-performed ultrasound in order to develop psychomotor skills acquisition. Images were obtained using a commercially available, ultra-portable, curvilinear US transducer and tablet computer. Each fellow obtained four 5-second ultrasound clips. A panel of expert ultrasound trainers reviewed images remotely for each fellow and provided individualized feedback on image adequacy and acquisition.

An image bank of 20 previously obtained representative lung US clips was assessed by the same panel and given a B-line score of 0-10. 10 scored clips were used as a training set for the fellows. The other 10 clips were scored by the fellows after the training program. Scores for each fellow were tested against the scores of the panel using interclass correlation coefficients which were confirmed using regression analysis. A Bland-Altman plot was constructed to analyze for bias. Paired two sample means t-test with a one-tailed p value were used to compare pre- and post-test scores.

Results

Surveys showed statistically significant increases in confidence in five domains critical to clinician-performed ultrasound. On the 5-point Likert scale confidence in psychomotor skills domain increased from a pre-test mean of 2.1 to a post-test mean of 4.3. Confidence in the knobology skills domain increased from a pre-test mean of 1.8 to post-test a mean of 4.1. Confidence in the image acquisition skills domain increased from a pre-test mean of 1.8 to a post-test mean of 3.9. Confidence in the image interpretation skills domain increased from a pre-test mean of 2.1 to a post-test mean of 4.2. Confidence in clinical integration increased from a pre-test mean of 2.7

Table 1. Clinician-Performed Ultrasound Domain Confidence Assessment. Assessment of confidence of nephrology fellows before and after a brief training course employing a 5-point Likert Scale.

Skills Domain Assessed	Pre-Course Mean	Post-Course Mean	p-value
Psychomotor	2.1	4.3	<0.001
Knobology	1.8	4.0	<0.001
Image Acquisition	1.8	3.9	<0.001
Image Interpretation	2.1	4.2	<0.001
Clinical Integration	2.7	4.3	<0.001
Aggregate	2.1	4.1	<0.001

to a post-test mean of 4.3. In the aggregate, confidence across the 5 skills domains increased from a pre-test mean of 2.1 to a post-test mean of 4.1. $P < 0.001$ for comparisons. Table 1. On the knowledge assessment, average score increased from 4% before the course to 92% after the course.

Comparing each fellow's scored clips to the expert panel's assessments, interclass correlation coefficients were 0.93, 0.93, 0.97, 0.97, 0.98, 0.95, 0.91, 0.75, 0.84, and 0.82 respectively for each fellow with an average of 0.90, and no scores below 0.75, demonstrating agreement in interpreting B-line scores which was confirmed on regression analysis. Bland-Altman demonstrated agreement with low bias. All user-generated images were reviewed as sufficient for clinical assessment by the expert trainers.

Discussion

Our results demonstrate increased nephrology fellow confidence in clinician-performed ultrasound across 5 critical domains following a brief training combining a web-based curriculum and short hands-on peer-mentored training. We showed ready uptake of critical knowledge for obtaining and interpreting quantitative studies. Further, the agreement of fellows' scores with an expert panel was excellent with high inter-rater reliability and minimal bias. These results expand on the work of Gargani, et al. demonstrating that nephrology fellows can be quickly trained in obtaining and interpreting quantitative lung US.

Conclusion

Clinician-performed quantitative lung US can be taught to nephrology fellows quickly and reliably. Further study is needed to determine whether training translates to clinical application and competence.

Disclosures

None

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Case File

Point of Care Ultrasound Diagnosis of Pseudoaneurysm of an Upper Extremity Arteriovenous Dialysis Graft

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Abstract

We describe the rapid diagnosis with point of care ultrasound (POCUS) of two acute pseudoaneurysms of a bovine arteriovenous dialysis graft with superimposed cellulitis in a 44-year old male patient who presented with pain over his upper arm graft site. POCUS evaluation decreased the time to diagnosis and vascular surgery consultation.

Case File

A 44-year old Hispanic male with a history of hyperlipidemia, methicillin sensitive staphylococcus bacteremia, and end stage kidney disease secondary to hypertension on hemodialysis with a left upper extremity arteriovenous graft presented to the Emergency Department with swelling and throbbing pain at the site of his graft for five days. The arteriovenous (AV), axillo-axillary, 6mm, bovine carotid graft was placed four months prior. Of note, the patient was hospitalized one month before presentation with suspected infection of the graft and was found to have MSSA bacteremia on the same encounter. He also had two other episodes of infection of prior grafts, one and three years earlier. Physical exam was notable for severe range hypertension with a blood pressure of 213/124 mm Hg, heart rate of 80 beats per minute, respiratory rate of 16 breaths per minute, SpO2 of 97% with an oral temperature of 36.8 °C. Exam of the left upper arm showed local erythema, tenderness and edema at the superior aspect of the AV graft with strong pulsatility and a continuous bruit.

Point of care ultrasound (POCUS) using a linear transducer revealed two pseudoaneurysms (Figure 1 and 4, online Video S1 and S2) of the graft that were not initially identified on physical exam due to severe tenderness on exam and tissue edema. After informing the patient of this finding, he revealed that he had in fact noticed two painful bumps develop immediately after his last dialyses session. The graft was otherwise patent without thrombus in the lumen. Each pseudoaneurysm appeared as a 4mm and 5mm defect within the graft wall, which is referred to as the neck of the pseudoaneurysm.

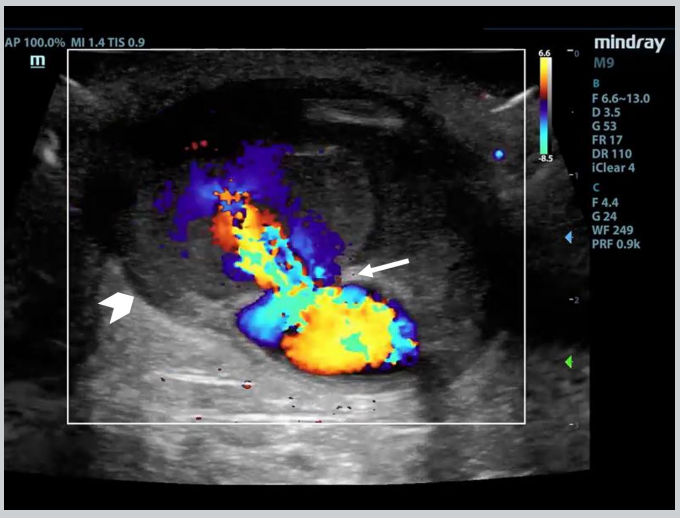

Figure 1. Short axis of AV graft can be seen with pseudoaneurysm neck (arrow) and sac (arrowhead). Color Doppler shows flow in graft and jet into pseudoaneurysm sac. Notice wall of graft is not continuous with wall of sac signifying pseudoaneurysm.

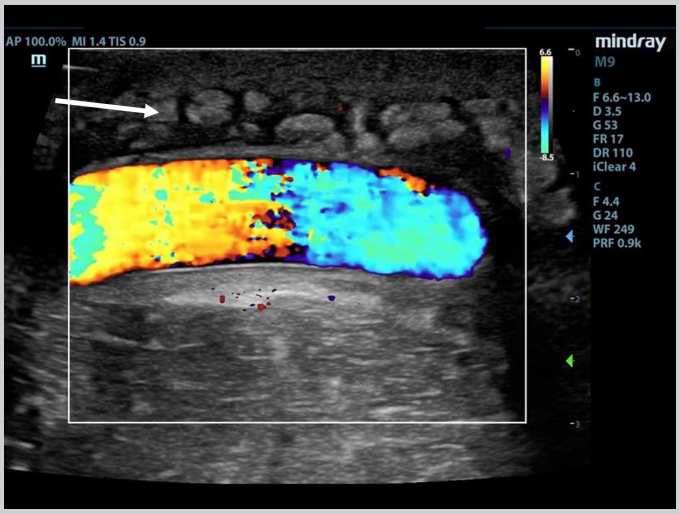

Figure 2. Patent segment of AV graft with cobblestoning (arrow) in the subcutaneous tissue suggestive of cellulitis.

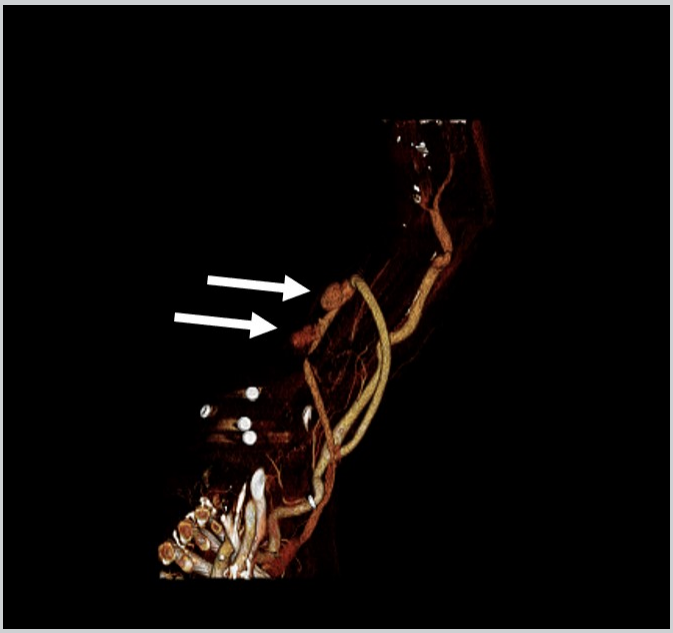

Figure 3. Reconstruction of computed tomography angiography of the left upper extremity with both pseudoaneurysm sacs visible adjacent to AV graft (arrows).

Figure 4. Short axis of AV graft can be seen with pseudoaneurysm neck and sac.

The neck led to a sac where blood could be seen swirling within the two similarly sized pseudoaneurysms on B-mode. Each measured approximately 1.5 x 3 x 3 cm. Color Doppler showed a pulsating jet entering the pseudoaneurysm from the neck (Figure 1). Additionally, cobblestoning of the subcutaneous tissue was observed directly adjacent to the graft at the proximal aspect, supporting the suspected underlying diagnosis of cellulitis (Figure 2). The patient was treated with vancomycin and cefazolin. POCUS prompted consultation of vascular surgery who removed the graft on day four of admission with a post-operative diagnosis of graft infection. Angiography with computed tomography was performed for preoperative planning (Figure 3). Surgical pathology showed myxoid degeneration of part of the graft wall. Tissue cultures from the graft site taken on the fourth day of antibiotic therapy were negative, including acid-fast bacilli, anerobic bacteria, and fungus. Gram stain was negative. Blood cultures drawn prior to antibiotic administration were negative. Transthoracic echocardiogram showed no valvular vegetations. The patient was discharged after eight days of hospital admission on cefazolin with a tunneled dialysis catheter.

A pseudoaneurysm is sometimes called a false aneurysm because it lacks all three normal elements of the arterial wall. The intima and media are disrupted and the adventitia acts as the outer layer of the pseudoaneurysm, which is why it is sometimes referred to as a contained rupture. The predominate risk is complete rupture, leading to life threatening bleeding or secondary infection. They are often caused by needle puncture and frequently associated with infection [1]. Pseudoaneurysm with pending rupture of AV grafts are relatively uncommon, accounting for an estimated 3% of AV graft failure, compared to 13% of AV fistula failure. The most common cause of AV graft failure is thrombosis and infection which account for 80% and 14% respectively [2]. Management requires vascular surgery consult for consideration of stent-graft placement or surgical repair with a bypass interposition graft around the site of the pseudoaneurysm. In cases of graft breakdown and infection, ligation or removal may be required. Angiographic examination or ultrasound can be used to assist in surgical planning [3].

Disclosures

The patient consented for use of ultrasound images and clinical information for academic purposes. The authors have no conflicts of interest to declare.

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Case File

Utility of Nephrologist-Performed Point of Care Ultrasonography in the Evaluation of Hyponatremia

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Abstract

Point of care ultrasonography can be a valuable adjunct to conventional physical examination in patients with hyponatremia that aids in clinical decision making. It can address the shortcomings of traditional volume status assessment such as the inherent low sensitivity of 'classic' signs such as lower extremity edema. Herein, we present a case of a 35-year-old woman where discrepant clinical findings led to confusion in the accurate assessment of volume status but addition of point of care ultrasonography helped to guide the therapy.

Case

Hyponatremia is the most common electrolyte disorder for which nephrology consultation is sought and represents an excess of water out of proportion to sodium. Accurate assessment of fluid volume status is paramount in appropriate management of hyponatremia. For example, both volume overload with decreased effective arterial volume and hypovolemia can act as stimulus for release of anti-diuretic hormone leading to hyponatremia, and the treatment is entirely different in both these scenarios. However, volume status assessment is not always straightforward owing to inherent low sensitivity of traditional physical examination signs as well as patient-related factors such as chronic lower extremity edema due to venous insufficiency [1-3]. In the recent past, point of care ultrasonography (POCUS) has emerged as a valuable adjunct to physical examination in the field of nephrology [4]. Rapid bedside sonographic assessment of the lung, inferior vena cava (IVC), heart, and abdominal venous Doppler waveforms in varying combinations depending on the clinical question can provide helpful insights into hemodynamics that can be integrated with conventional assessment to guide management.

We recently cared for a 35-year-old woman with hyponatremia in whom POCUS aided in the accurate assessment of volume status. The patient had a history of developmental delay as well as a disabling connective tissue disorder with upper limb contractures and heart failure with preserved ejection fraction. She initially presented to the hospital for worsening lower extremity edema compared to her usual state. Her home dose of loop diuretic was furosemide 20 mg as needed. Laboratory data was significant for a serum sodium of

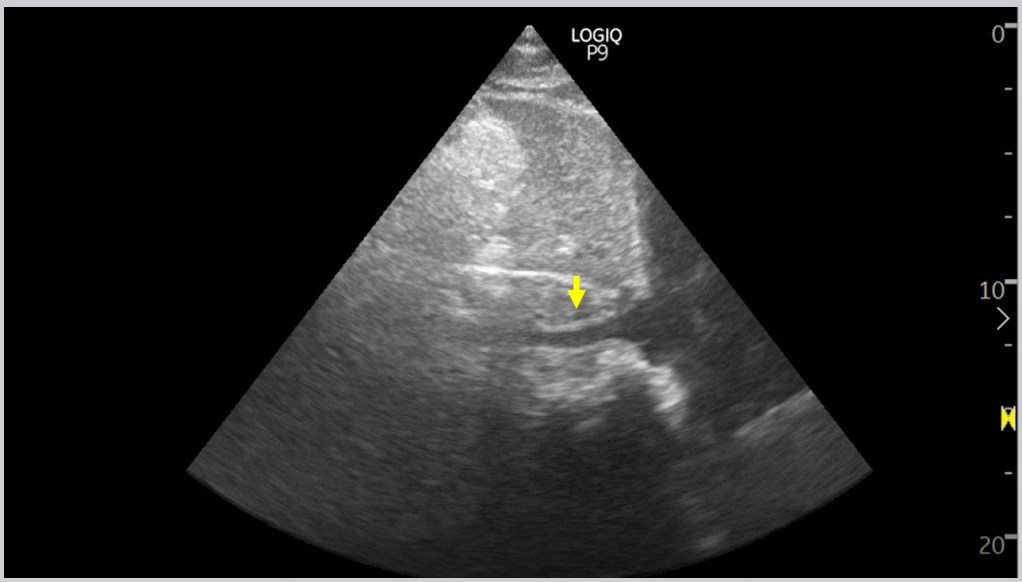

Figure 1. Sonographic image demonstrating a small inferior vena cava (maximal diameter). Online Video S1 demonstrates the respiratory variation. Image was obtained using a phased array transducer from the subxiphoid window with the probe orientation marker towards patient's head.

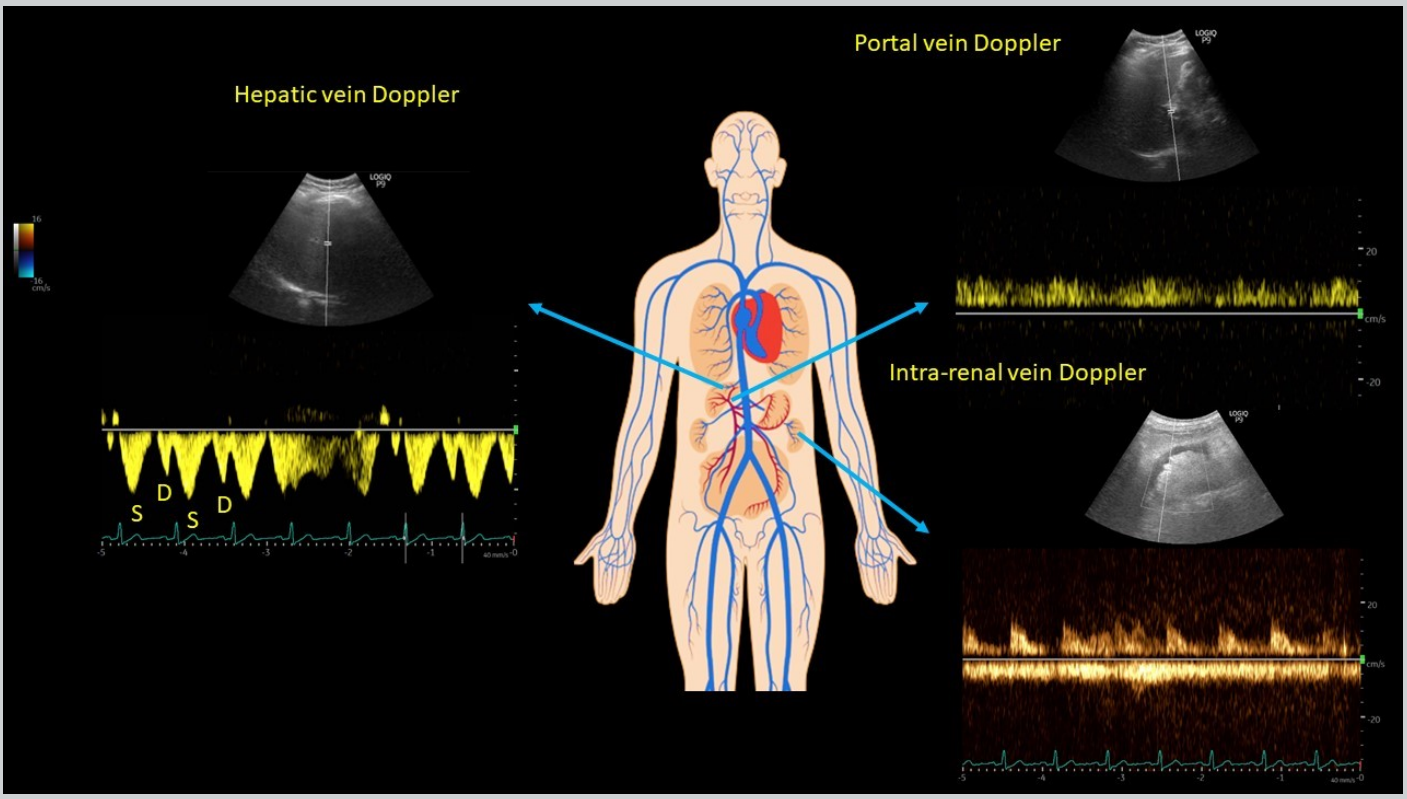

Figure 2. Venous Doppler images demonstrating normal hepatic, portal, and intra-renal vein waveforms. In hepatic vein, S = systolic wave, D = diastolic wave (normally, S is greater than D). For portal and intra-renal veins, a continuous pattern without distinct S and D waves is considered normal. Images were obtained using a curvilinear transducer from the lateral aspect, just below the diaphragm. Pulsed-wave Doppler was utilized to obtain the waveforms with simultaneous EKG gating. *Human body image licensed from shutterstock ®*

122 mEq/L (baseline: 128-130), serum osmolality 257 mOsm/kg, and a normal serum creatinine. She was treated with intravenous loop diuretics for exacerbation of heart failure and the serum sodium improved to 127 mEq/L over the next two days. Serum creatinine was relatively stable at 0.8 mg/dL. However, the sodium level subsequently declined with continued diuretic therapy and reached a value of 121 mEq/L. Nephrology was consulted for evaluation and management of hyponatremia at that time. Urine osmolality and spot urine sodium were obtained which were 259 mOsm/kg and 70 mmol/L respectively. Physical examination was significant for bilateral 2+ pitting pedal edema, but auscultated lung zones were clear. Chart review revealed a weight gain of 2 kg during the hospitalization. Based on this data, there was a discrepancy in opinion among the treating physicians about her volume status. We performed point of care ultrasound which revealed a small IVC less than 1 cm in maximal diameter with 100% collapse with inspiration suggestive of low right atrial pressure (Figure 1, online Video S1). Lung ultrasound did not reveal B-lines. Cardiac Doppler to assess fluid responsiveness could not be performed due to difficult body habitus. A venous excess Doppler ultrasound (VExUS) evaluation was performed to exclude systemic venous congestion which revealed normal waveforms in the hepatic, portal, and intra-renal veins (Figure 2). Based on these findings, hypervolemic hyponatremia was thought to be unlikely and the loop diuretics were held. In addition, fluid intake was liberalized. The serum sodium improved to 127 mEq/L over the next two days and the patient was discharged.

Through this case, we would like to convey that POCUS can be used as a supplement to physical examination, laboratory data and other clinical parameters to evaluate volume status, and guide therapy in patients with hyponatremia. In addition, while one may question the utility of VExUS scan when the IVC is small [5], we do it in two situations. First, we use VExUS in patients with limited acoustic windows, where IVC ultrasound is prone to errors such as mistaking aorta or caudate lobe of the liver for IVC. Second, we use VExUS in those with discrepant clinical data such as our patient who had a discrepancy in weight change as well as lower extremity edema which was felt due to factors other than volume overload.

Conflict of Interest

The authors have declared that no conflict of interest exists.

Patient consent

Informed consent was obtained from the patient's guardian to publish this case study. No identifiable information included.

Authorship

All the authors have made substantial contribution to the preparation of this manuscript.

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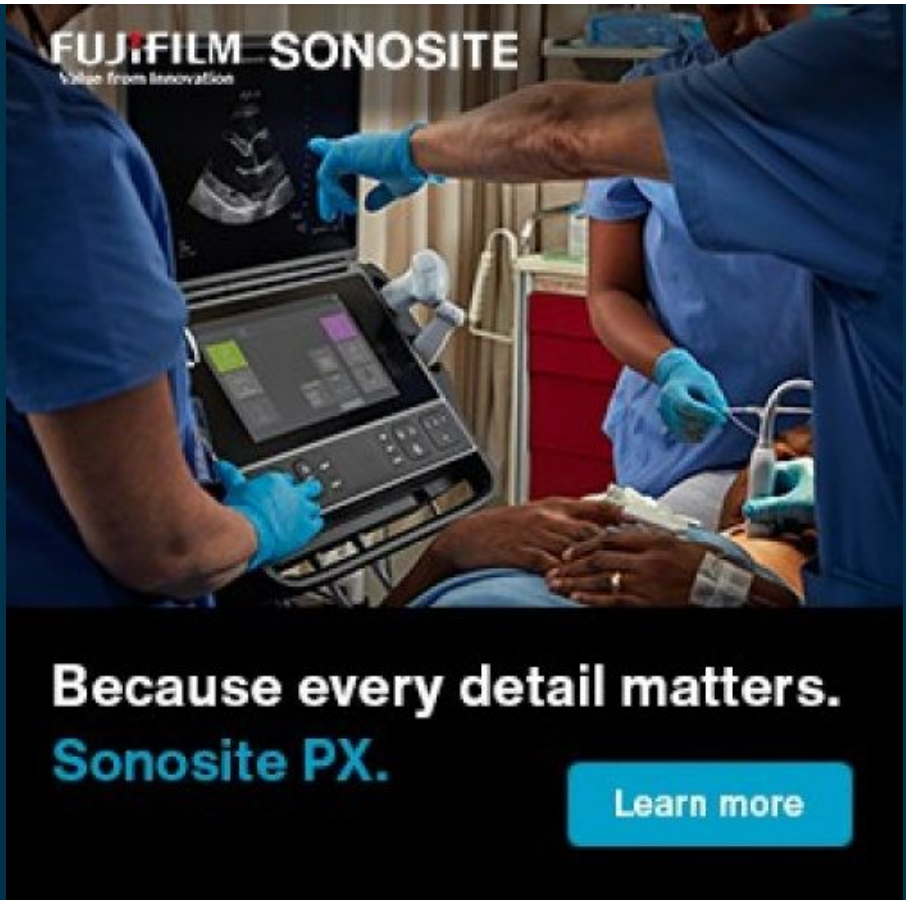

Point of Care Ultrasonography to Monitor Decongestive Therapy in Heart Failure: Seeing is Believing

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Abstract

Point of care ultrasonography (POCUS) is a non-invasive bedside diagnostic tool that aids in clinical decision-making process. In addition, it allows to monitor the efficacy of therapeutic interventions in real time. As such, nephrologists can enhance patient care by adopting this skill, especially in those with simultaneous cardiac dysfunction and difficult to manage fluid status. Herein, we present a case of heart failure and hypotension, where POCUS helped guide the management as well as visualize the effect of ultrafiltration therapy on circulatory pathophysiology.

Case

Point of care ultrasonography (POCUS) is increasingly being used as an adjunct to physical examination in internal medicine and subspecialties. In nephrology practice, it is particularly valuable in the objective assessment of fluid volume status. In addition, POCUS enables the physicians to better appreciate the anatomic and pathophysiologic changes that occur during the course of patient management. The intent of this case file is to demonstrate the improvement in sonographic markers of congestive state during ultrafiltration therapy in a patient with heart failure.

A 74-year-old gentleman with a history of hypertension, diabetes mellitus type 2, coronary artery disease, congestive heart failure with reduced left ventricular ejection fraction (<20%), and chronic kidney disease stage 3 was admitted to the hospital for acute exacerbation of heart failure. He presented with a serum

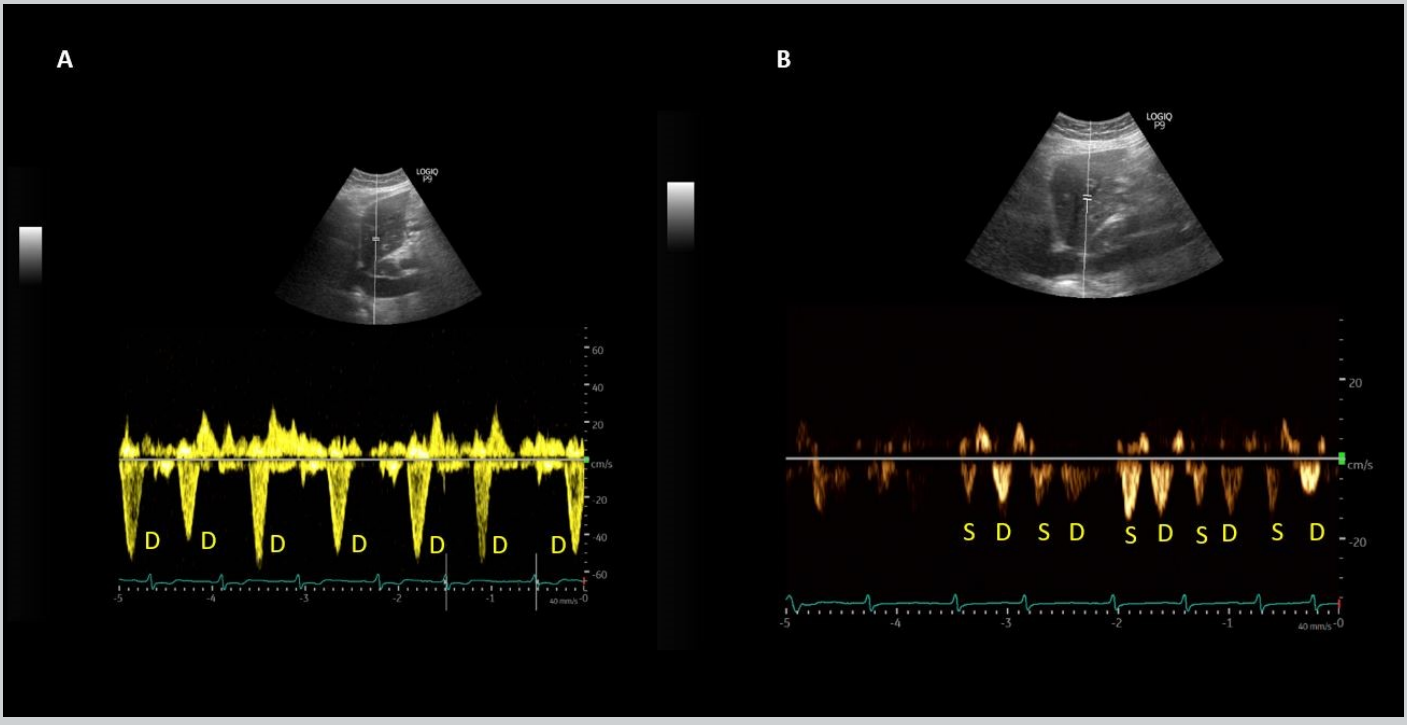

Figure 1. A) Hepatic vein Doppler waveform at the initiation of ultrafiltration therapy demonstrating only diastolic (D) wave below the baseline indicating severe congestion. B) Follow up waveform demonstrating both systolic (S) and diastolic (D) waves below the baseline, indicating improved venous return. Note the correlation with accompanying EKG.

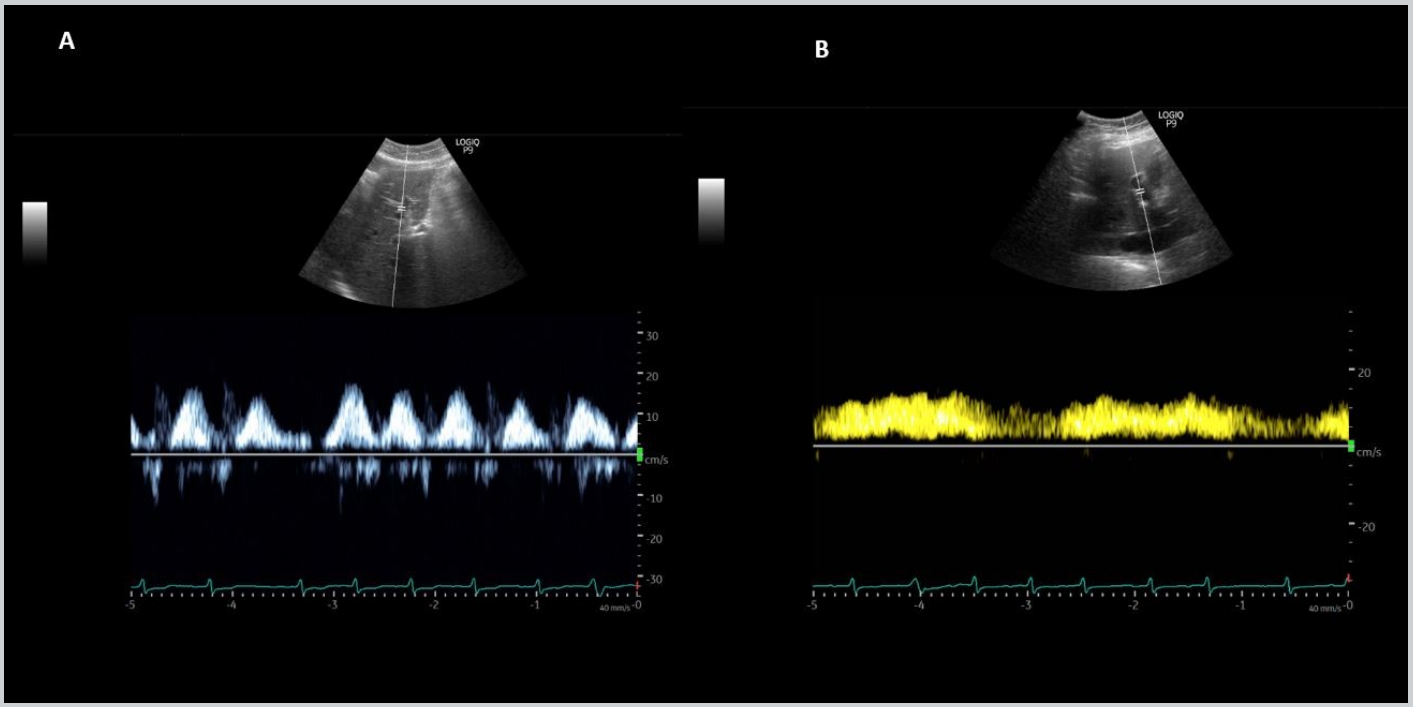

Figure 2. A) Portal vein Doppler waveform at the initiation of ultrafiltration therapy demonstrating pulsatile pattern consistent with severe congestion. B) Follow up waveform demonstrating considerable improvement in the pulsatility (almost normal, continuous pattern).

creatinine of 2.7 mg/dL, which slowly trended down to 2.3 mg/dL with intravenous loop diuretic therapy over the next 5 days and started to trend up again prompting nephrology consultation. As the serum creatinine continued to rise (4.1 mg/dL) with oliguria and hypotension (systolic blood pressure 85-90 mmHg), continuous renal replacement therapy was initiated. He was also started on dobutamine drip by the cardiology team. A POCUS examination was performed by the nephrologist including a focused echocardiogram, lung ultrasound, and a venous excess Doppler ultrasound (VExUS). Echo was significant for a plethoric inferior vena cava (IVC) measuring approximately 2.5 cm in maximal diameter (online Video S1A) with almost no respiratory variation consistent with very high right atrial pressure. There was significantly decreased left ventricular ejection fraction. Parasternal short axis view demonstrated a 'D'-shaped left ventricle with interventricular septal flattening throughout the cardiac cycle suggestive of right ventricular pressure and volume overload (online Video S1B). It was likely that the compression of the left ventricle was leading to a reduction in stroke volume, contributing to hypotension. Lung ultrasound demonstrated B-line pattern bilaterally, consistent with pulmonary edema/interstitial syndrome (online Video S1C). VExUS scan demonstrated D-only pattern on hepatic vein Doppler, which means there is flow towards the heart only during diastole (severe congestion, Figure 1A). Similarly, portal vein Doppler was suggestive of severe congestion with 100% pulsatility and possible flow reversal during systole (Figure 2A). Based on these findings, the rate of ultrafiltration was increased despite hypotension and the patient was intubated soon after this scan was performed. A repeat POCUS examination was performed 4 days later after approximately 10 liters net ultrafiltration. The patient remained intubated at that time though the systolic blood pressure improved to ~110 mmHg. Inferior vena cava was still plethoric (on mechanical ventilation, online Video S2A) but the venous Doppler showed significant improvement in hepatic and portal vein waveforms. Both S (systolic) and D (diastolic) waves were below the baseline on the hepatic vein tracing indicating near-normal venous return (Figure 1B) and the portal vein pulsatility has substantially improved to ~30% (Figure 2B). Interestingly, the left ventricle appeared round on the parasternal short axis view suggesting improvement in right ventricular volume and pressure overload and thus improved left ventricular outflow (online Video S2B). As expected, lung ultrasound showed improvement with predominantly A-line pattern though there were B-lines at the bases (online Video S2C). In addition, the urine output also picked up though the patient was never completely anuric.

In summary, it is important for the nephrologists to be aware that not all hypotension is due to volume depletion

and cases of severe congestion with dilated right ventricle compromising the left ventricular outflow as demonstrated here will respond to volume removal [1, 2]. In addition, flow patterns in hepatic and portal veins (renal parenchymal vein where feasible) can be used to monitor the efficacy of decongestive therapy [3-6] in real time, even in cases where the inferior vena cava remains enlarged due to chronic pulmonary hypertension and/or positive pressure ventilation.

Conflict of Interest

The author declares that no conflict of interest exists.

Consent

Informed consent has been obtained from the patient for the publication of this case study.

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Case File

Evaluation of Venous Congestion Using Beside Ultrasonography by the Nephrology Consultant: The VExUS Nexus

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Abstract

In patients with heart failure and cardiorenal syndrome, lingering congestion is associated with worse outcomes. As such, titrating diuretic or ultrafiltration therapy based on objective assessment of volume status plays a crucial role in the management of these patients. Conventional physical examination findings and parameters such as daily weight measurement are not always reliable in this setting. Recently, point of care ultrasonography (POCUS) has emerged as an attractive enhancement to bedside clinical examination in assessing fluid volume status. Specifically, Doppler ultrasound of the major abdominal veins gives additional information about end-organ congestion when used in conjunction with inferior vena cava ultrasound. Moreover, these Doppler waveforms can be monitored in real time to gauge the efficacy of decongestive therapy. Herein, we present a case that illustrates the utility of POCUS in the management of a patient with heart failure exacerbation.

Case

A 62-year-old man with a history of diabetes mellitus type 2, coronary artery disease, heart failure with reduced left ventricular ejection fraction (approximately 20%), and stage 3 chronic kidney disease was admitted to the hospital for management of right lower extremity ulceration possibly requiring an above-knee amputation. His home medications were resumed including the loop diuretic, bumetanide 2mg twice a day. Serum creatinine at presentation was 2.4 mg/dL (baseline ~1.6 - 1.8), which increased to 3.2 mg/dL over the next 2 days. Nephrology was consulted for acute kidney injury. The documented weight was 66.8 kg, which decreased by 6 kg compared to that of previous day. Notably, the weighing equipment was different as the patient was transferred to a different ward. Cardiopulmonary examination was unremarkable except for basal crackles and mild jugular venous distension. There was trace pedal edema on the left and right leg showed the known ulceration with surrounding inflammation. The patient was a poor historian and endorsed ‘feeling fine’ without the need for supplemental oxygen. We were asked if the patient was ‘overdiuresed’ based on the reduction in weight accompanied by rise in serum creatinine.

A point of care ultrasound (POCUS) examination was performed to elucidate the fluid volume status and guide management. Focused echocardiogram was notable for reduced left ventricular systolic function with global hypokinesis, moderate right ventricular enlargement without obvious interventricular septal flattening, and trace tricuspid regurgitation. There was trace pericardial effusion. Inferior vena cava (IVC) was dilated with a maximal diameter of ~2.5 cm and minimal respiratory variation consistent with a right atrial pressure of at least 15 mmHg. Lung ultrasound demonstrated 3 or more B-lines per rib-interspace in the examined zones bilaterally. A venous excess ultrasound (VExUS) grading was performed at the same time. Hepatic vein spectral Doppler waveform revealed only diastolic (D) wave below the baseline with systolic (S) flow reversal. Portal vein Doppler revealed 100% pulsatility with flow reversal during systole and intra-renal waveform showed flow only during diastole, i.e., only D-wave below the baseline (Figure 1). Taken together, these findings were consistent with severe systemic venous congestion as well as pulmonary congestion in the setting of heart failure exacerbation. Figure 2 illustrates the normal Doppler waveforms and their transformation with elevated right atrial pressure. The diuretic therapy was intensified, and the serum creatinine improved to 2.1 mg/dL during the next 4 days. The portal vein waveform was almost normalized during this period (Figure 3), though hepatic and intra-renal vein continued to show congestive pattern albeit with subtle changes suggesting improvement in right atrial pressures. For example, amplitude of the systolic flow reversal has reduced in the hepatic vein and systolic flow started to appear below the baseline in the intra-renal vein. IVC remained >2 cm in diameter but the degree of inspiratory collapse has improved. However, the serum creatinine worsened to 2.7 mg/dL 2 days later, and at the same time, he underwent right above-knee amputation. Intra-operatively, he developed forward failure requiring ionotropic therapy and subsequently developed oliguric renal failure requiring continuous renal replacement therapy. Inotropes were weaned off in one day and mechanical fluid removal was continued. Pre-operative rise in creatinine despite improving congestion

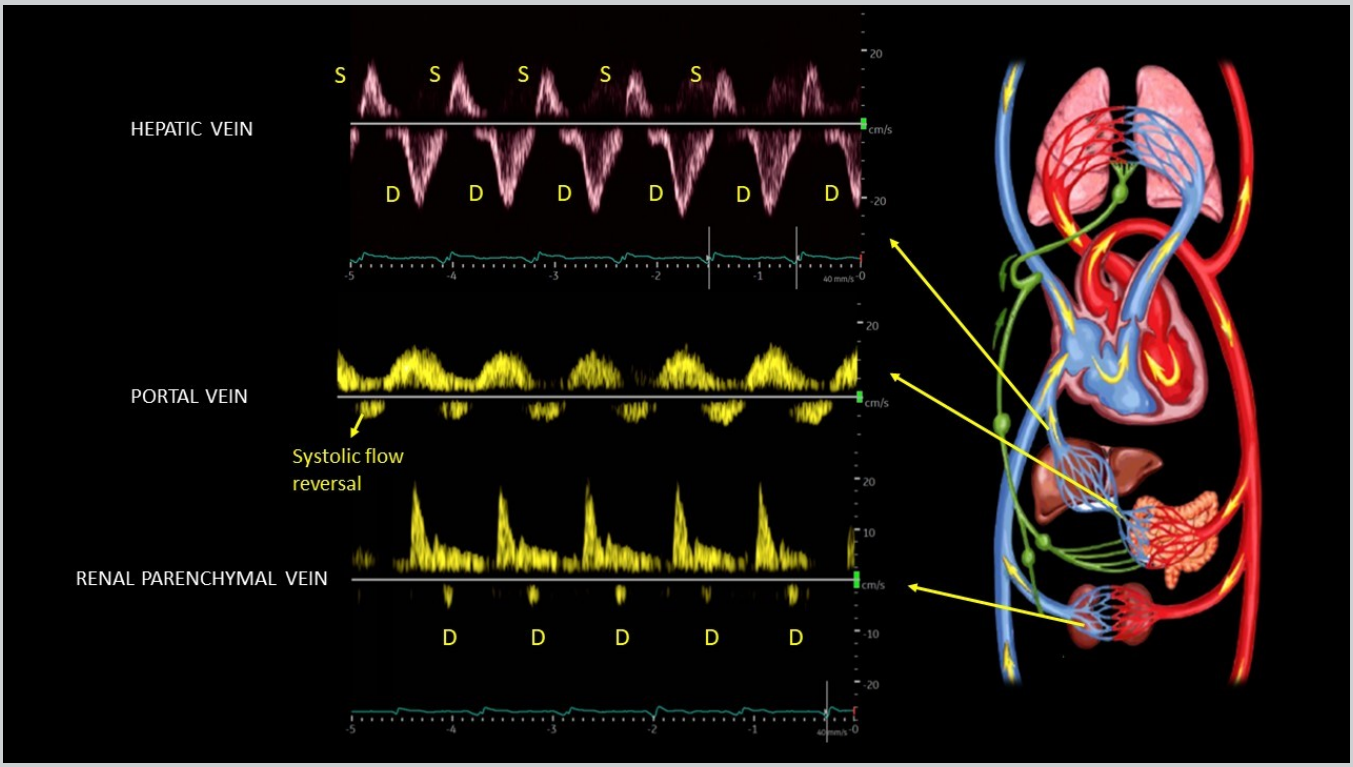

Figure 1. Venous Doppler images at the time of initial POCUS scan demonstrating severe congestive pattern in hepatic, portal, and renal parenchymal veins. There is flow reversal during systole (flow away from the heart) in all the three veins. S = systolic wave; D = diastolic wave. *Hemodynamic circuit illustration licensed from shutterstock®*

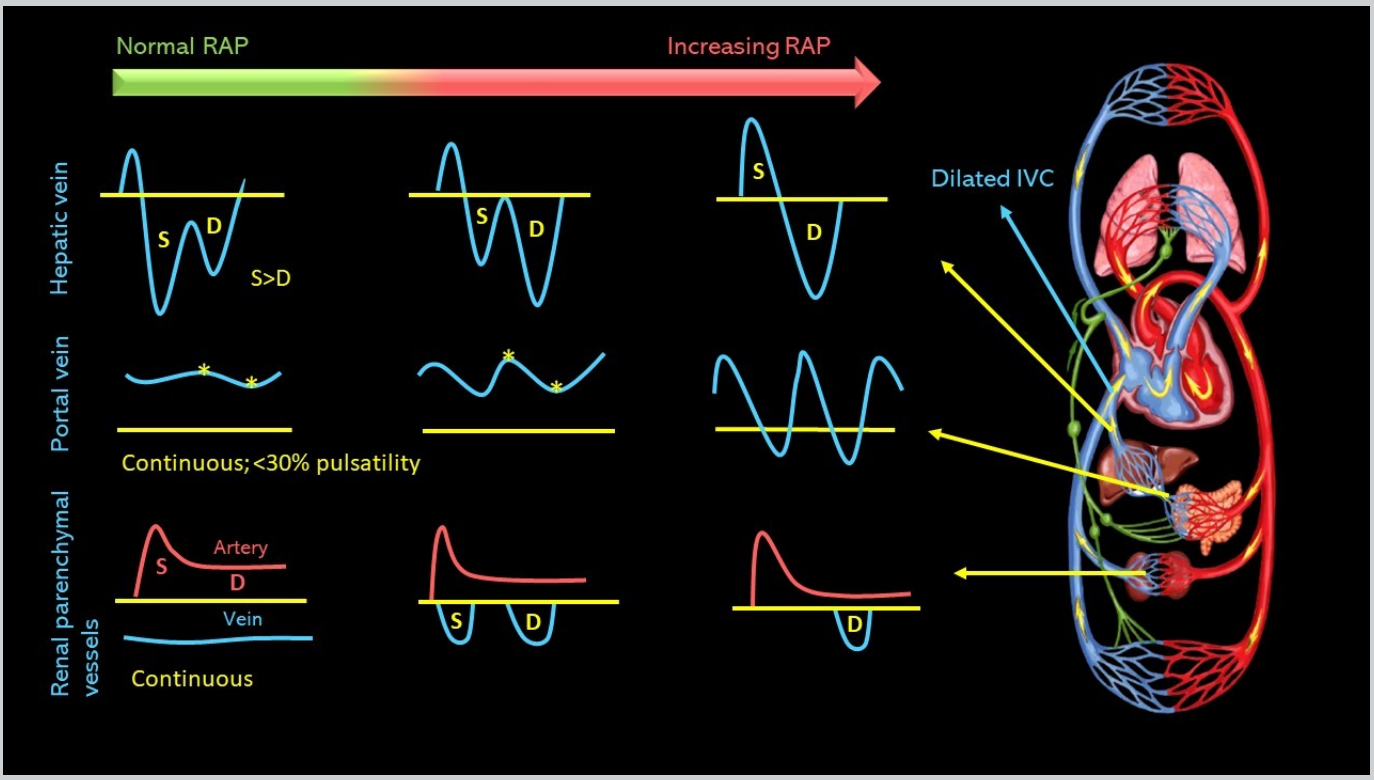

Figure 2. Illustration showing the natural history of venous Doppler waveforms with increasing right atrial pressure. Dilatation of the inferior vena cava (typically >2 cm) usually precedes these changes. S = systolic wave, D = diastolic wave. Asterisks on the portal vein waveform indicate the highest and lowest amplitudes during a given cardiac cycle used to calculate percent pulsatility. *Note that the normal portal vein waveform is above the baseline and the renal is below, which reflects the direction of blood flow towards and away from the transducer, respectively.*

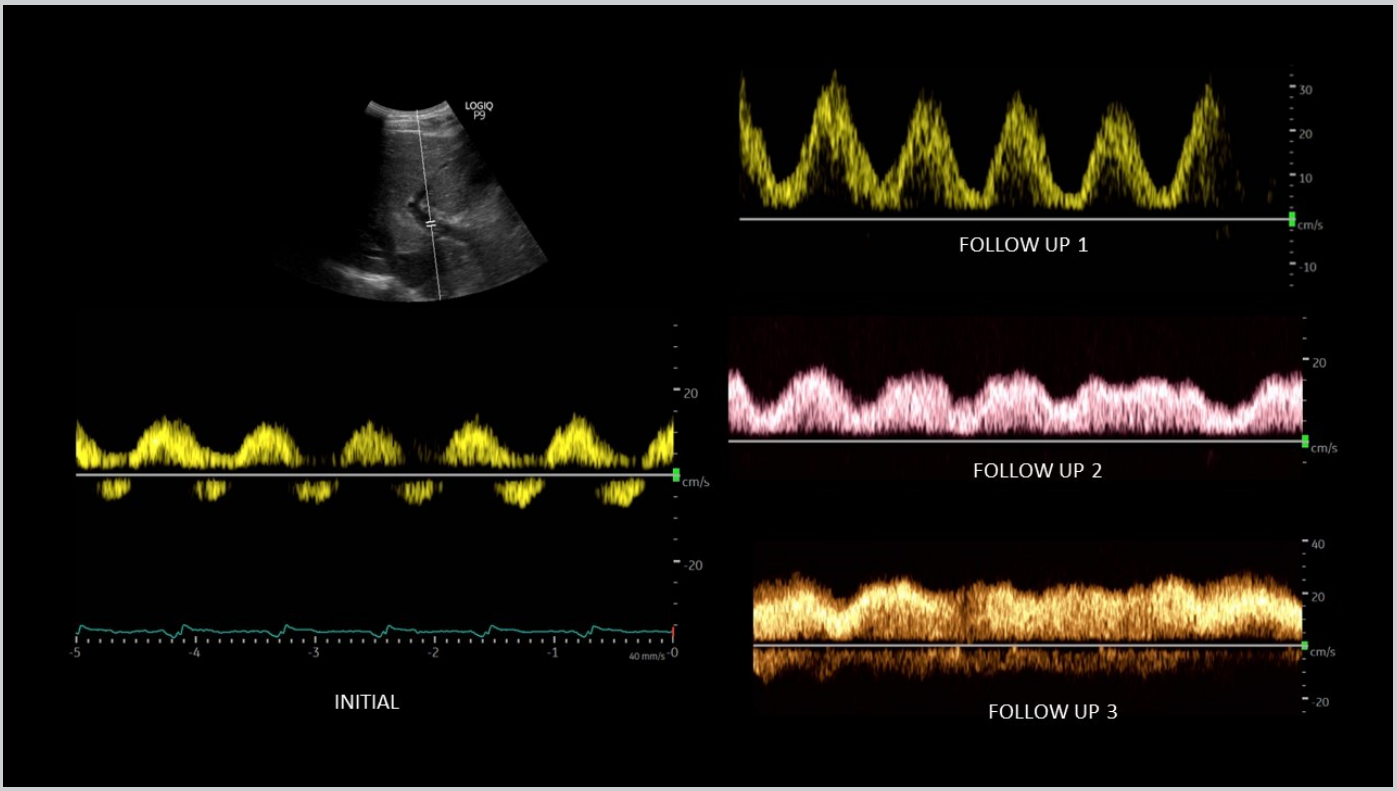

Figure 3. Changes in portal vein waveform in response to decongestive therapy. Note that the systolic flow reversal has disappeared initially followed by gradual decrease in pulsatility.

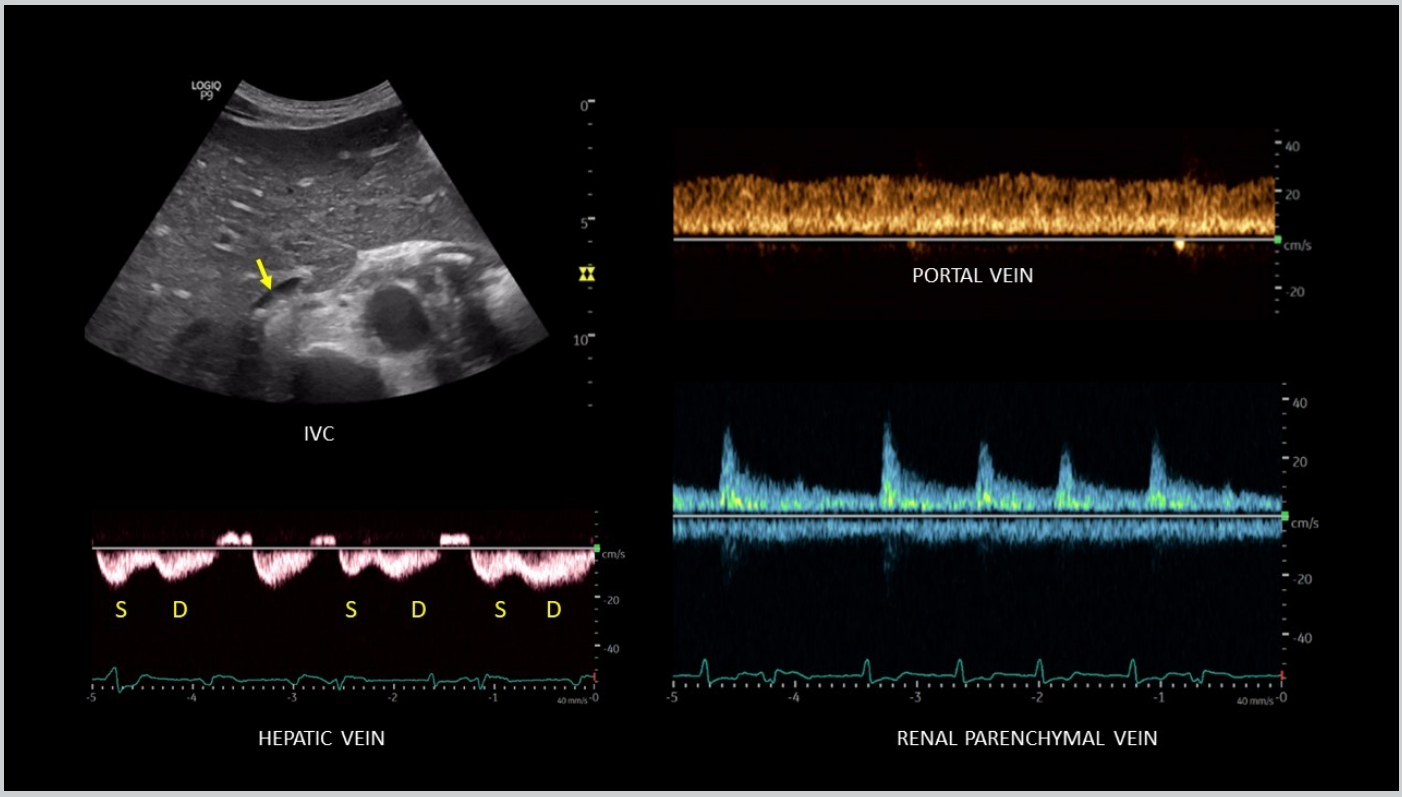

Figure 4. Small inferior vena cava and normalized venous Doppler waveforms following decongestive therapy. Hepatic waveform shows both S and D components below the baseline in most cardiac cycles and portal and renal waveforms are continuous. Note that the patient had atrial fibrillation at the time of this scan, which decreases the amplitude of S wave.

was likely secondary to cardiac pump failure. On post-operative day 10 and prior to discharge, a repeat POCUS examination showed a small collapsible IVC as well as normalization of all the venous Doppler waveforms (online Video S1, Figure 4), indicating the resolution of the venous congestion. In addition, lung ultrasound demonstrated A-line pattern in the sono-auscultated zones.

The take-home points from this case file are:

Doppler ultrasound of the hepatic, portal, and intra-renal veins can be used as an adjunct to inferior vena cava ultrasound and other parameters such as body weight to assess venous congestion in patients with heart failure. Having a simultaneous electrocardiographic tracing helps with accurate interpretation of the waveforms by delineating the phases of cardiac cycle.

These venous waveforms reflect the end-organ congestion and in fact, have shown to outperform isolated central venous pressure (CVP) in predicting the risk of acute kidney injury in selected patients [1].

VExUS scans can be used to monitor the efficacy of decongestive therapy in heart failure patients. As demonstrated in this case, portal vein waveform typically improves the other waveforms as well as the IVC distension likely because of the 'partial' transmission of CVP to hepatic sinusoids due to the resistance offered by hepatic venous sphincters [2].

If the serum creatinine worsens despite improvement in the venous waveforms, impairment of the forward flow should be suspected and managed accordingly. On a similar note, caution must be exercised in patients with chronic pulmonary hypertension, where overzealous attempts to normalize all the waveforms may lead to decreased preload and consequent pump failure. Having a baseline VExUS grade helps in such cases, if available.

Conflict of Interest

The author declares that no conflict of interest exists.

Consent

Informed consent has been obtained from the patient for the publication of this case study.

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Case File

Massive Lymphocele Associated with Allograft Hydronephrosis: An Ultrasound Case Study

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Abstract

Lymphocele is a lymphocyte-rich fluid collection that results from disruption of lymphatics in the recipient during renal transplantation. While small collections resolve spontaneously, larger, symptomatic ones may cause obstructive nephropathy requiring percutaneous or laparoscopic drainage. Prompt diagnosis using bedside sonography may obviate the need for renal replacement therapy. Herein, we present a case of a 72-year-old kidney transplant recipient who developed allograft hydronephrosis secondary to compression by a lymphocele.

Case File

A 72-year-old woman with a history of end-stage kidney disease underwent deceased donor kidney transplantation with a cold-ischemia time of 21 hours. Basiliximab was used for induction immunosuppression (IS), followed by maintenance IS consisting of mycophenolate mofetil, tacrolimus, and prednisone. Despite good urine output, her serum creatinine remained high ~4mg/dL and allograft biopsy demonstrated severe donor disease with arteriosclerosis, interstitial fibrosis, and tubular loss, though it excluded rejection. 20-days post-transplant, she developed oliguric renal failure requiring renal replacement therapy. A bedside renal sonogram demonstrated moderate hydronephrosis of the renal allograft secondary to compression of the transplanted ureter by a large anechoic fluid collection in the pelvis (Figure 1). Computed tomography (CT) scan confirmed the same (Figure 2) and the patient underwent ultrasoundguided drainage of approximately 450 cc fluid the next day with drain placement leading to improvement in urine output. Laboratory analysis of the fluid was consistent with lymphocele and a repeat sonogram showed significant improvement (Figure 3). One month later, the patient required a laparoscopic peritoneal window for drainage of the lymphocele into the peritoneal

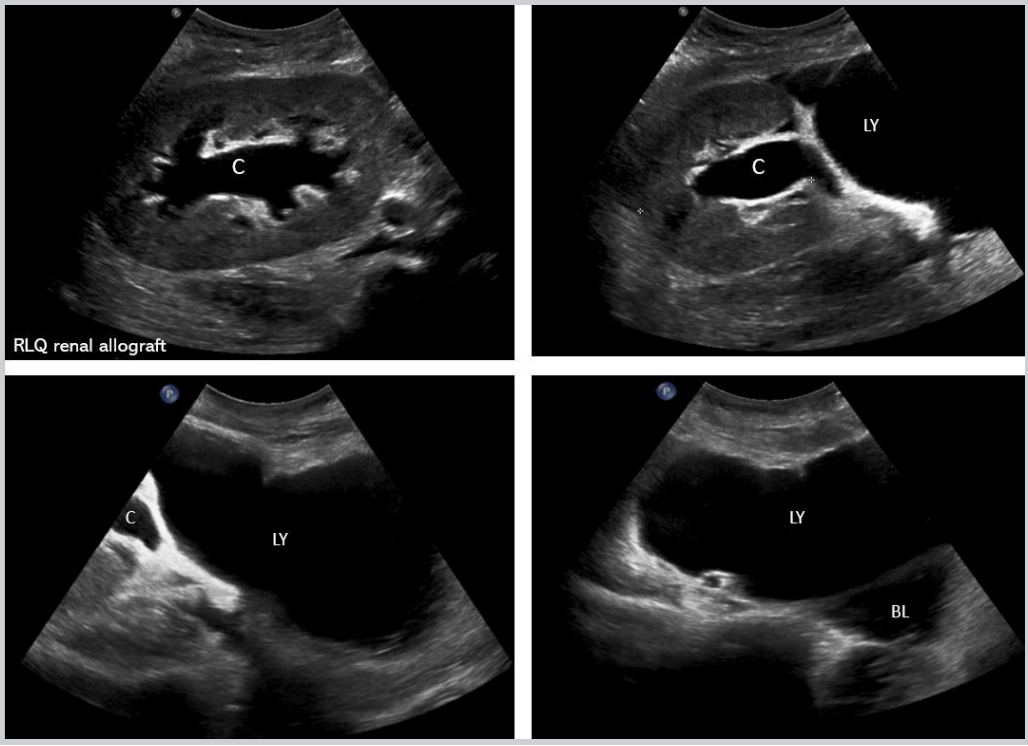

Figure 1. Sonographic images demonstrating a large hypoechoic collection (lymphocele) compressing the ureter and leading to hydronephrosis. Note the relationship between the lymphocele, renal collecting system, and the urinary bladder. RLQ = right lower quadrant; LY = lymphocele; C = renal collecting system; HY = hydronephrosis; BL = urinary bladder

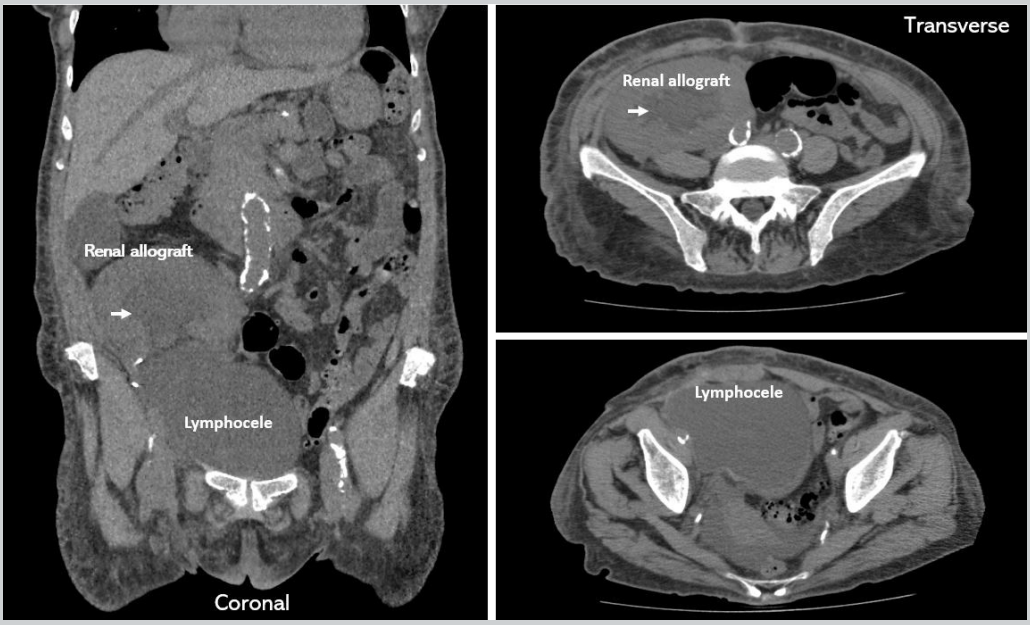

Figure 2. Computed tomography (CT) scan of the abdomen and pelvis without contrast demonstrating a large lymphocele occupying most of the pelvis. Arrows point to dilated renal collecting system/hydronephrosis.

cavity, during which time, the drain was removed. The serum creatinine stabilized around 2.1mg/dL gradually over a month.

A lymphocele typically occurs due to extravasation of lymph from the injured lymphatic vessels during preparation of the iliac vessels of the recipient and unligated lymphatics from renal hilum of the donor. These collections may develop in the early postoperative period or months following transplantation [1]. The introduction of ultrasound evaluation has contributed to increasing the diagnosis and consequently the incidence of lymphocele especially of the asymptomatic ones. Before ultrasound examination, the incidence ranged from 0.6 to 18.1% [2]. Small lymphoceles resolve spontaneously while the larger symptomatic ones may need percutaneous drainage or laparoscopy, with the later having least chance of recurrence [3]. Sonographically, they appear as anechoic fluid collections around the allograft and must be distinguished from the adjacent urinary bladder and renal cysts. Rescanning after emptying the bladder aids in differentiating from the bladder. Renal cysts are typically well-circumscribed and connection with the renal parenchyma can be demonstrated. Moreover, history of kidney cysts in the donor kidney should be readily available, especially in the early post-transplant period. Some lymphoceles may also demonstrate internal septations and appear as multilocular cystic structures.

In addition to rejection, structural abnormalities should be considered in renal transplant recipients with acute kidney injury, which are readily identifiable on a bedside sonographic examination in most cases.

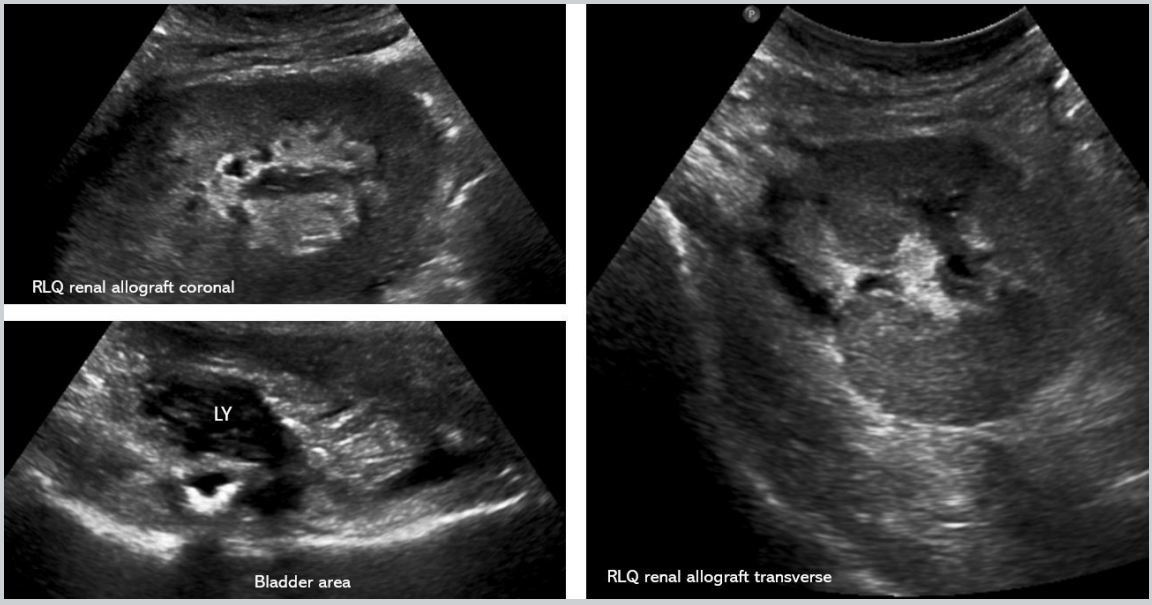

Figure 3. Repeat sonogram after the intervention demonstrating significant improvement in hydronephrosis and lymphocele.

Statement of Ethics

Informed consent obtained from the patient to publish this manuscript.

Conflict of Interest

The authors have declared that no conflict of interest exists.

Authorship

All the authors have made substantial contribution to the preparation of this manuscript. HB: drafted the manuscript and performed literature search; KFA: attending physician on the case, directed patient care; AK: procured the images, critically reviewed, and revised the manuscript for important intellectual content.

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POCUS Allows for Rapid Elucidation of Acute Kidney Injury in a Patient with Progressive Multiple Myeloma

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Abstract

A 63-year-old man with past history of multiple myeloma recently started on a regimen of daratumumab, carfilzomib, and dexamethasone was referred to our emergency department for a rapidly rising serum creatinine as high as 10 mg/dL. He complained of fatigue, nausea, and poor appetite. Exam revealed hypertension, but no edema or rales. Labs were consistent with AKI without hypercalcemia or evidence of hemolysis or tumor lysis. Urinalysis and urine sediment were bland without proteinuria, hematuria, or pyuria. Initial concern was for hypovolemia or myeloma cast nephropathy. POCUS revealed no overt evidence of volume overload or depletion, instead revealing bilateral hydronephrosis. Bilateral percutaneous nephrostomies were placed with resolution of the AKI. Ultimately, referral imaging revealed interval progression of bulky retroperitoneal extramedullary plasmacytomas compressing the ureters bilaterally related to the underlying multiple myeloma.

Case

A 63-year-old man with past medical history of advanced IgG Kappa multiple myeloma presented with worsening fatigue, nausea, and loss of appetite. He had progression of disease despite completion of multiple prior therapies for myeloma including autologous stem cell transplant and three weeks prior to presentation was started on combination therapy with daratumumab, carfilzomib, and dexamethasone. Subsequently, he had waxing and waning levels of energy and decreased oral intake. He denied lightheadedness, abdominal pain, vomiting, rash, and joint pain. He denied any urinary complaints and noted no change in urine output. He noted some loose stools. He had weekly outpatient labs and was noted to have a rising serum creatinine (Cr) from 1.6 mg/dL to 3.8 mg/dl one week prior to presentation. Repeat labs the day of presentation demonstrated a Cr of 9.3mg/dL and the patient was instructed to present to the emergency department for further evaluation.

On arrival, the patient's vitals were: blood pressure 176/109 mmHg, heart rate 64 beats per minute, oxygen saturation 99% on room air, and temperature of 36.9C.

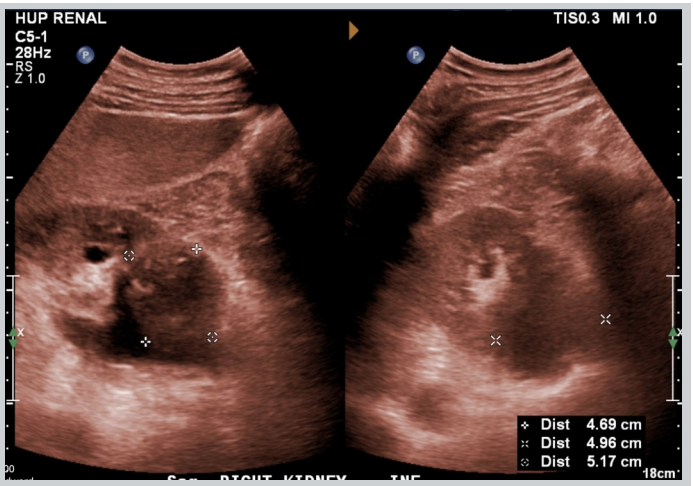

Figure 1. Confirmatory referral kidney ultrasound by radiology in sepia tone demonstrating hypoechoic 5.2 cm retroperitoneal lesions likely representing extramedullary plasmacytomas compressing the proximal ureter. Left: right kidney long axis. Right: right kidney short axis.

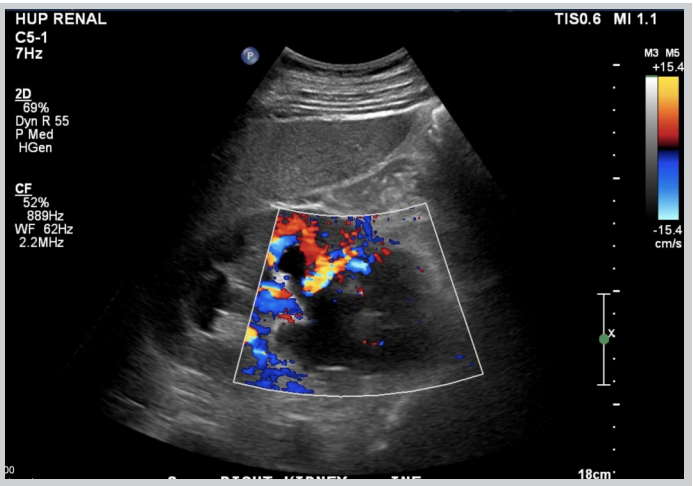

Figure 2. Doppler imaging of right kidney, long axis demonstrating absence of flow in the dilated renal pelvis, proximal ureter, and masses in the retroperitoneum at the inferior pole.

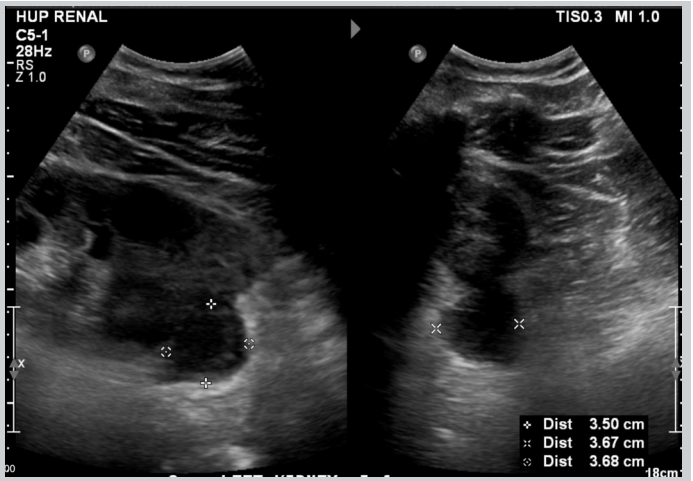

Figure 3. Referral kidney ultrasound of left kidney in long axis demonstrating suspected plasmacytomas 3.7 cm in maximum diameter at the inferior pole. Left: left kidney long axis. Right: left kidney short axis.

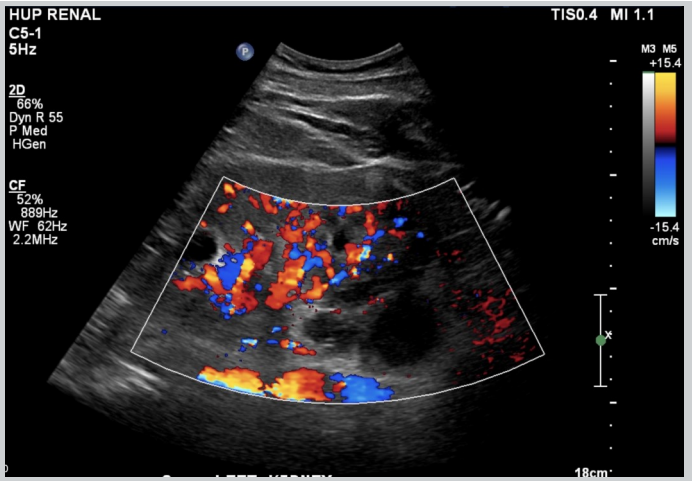

Figure 4. Doppler imaging of left kidney in long axis demonstrating lack of fast flow in the area of suspected plasmacytomas.

Physical exam demonstrated moist mucous membranes and good skin turgor. Jugular veins were not well-visualized. Axillary sweat was present. Pulmonary crackles and lower extremity edema were absent. There was no costovertebral angle tenderness.

Initial labs confirmed elevated blood urea nitrogen (91mg/dl) and creatinine levels (10.76 mg/dl). Other labs were notable for serum sodium of 138 mmol/dL, potassium elevated at 5.5 mmol/dL, bicarbonate low at 17 mmol/dL, calcium normal at 8.7 mg/dL (with normal albumin), and phosphate elevated at 8.7 mg/dL. Lactate dehydrogenase and uric acid were only mildly elevated at 200 units per liter and 10.8 mg/dL respectively. Complete blood count revealed white blood cells of 4400 per µL, hemoglobin of 10.3 g/dL, and platelets of 6300 per µL. Urinalysis was negative for heme, albumin, and leukocyte esterase with bland sediment. Quantitative serum kappa free light chains were 203.8 mg/L and quantitative serum lambda free light chains were 6.5 mg/L with kappa to lambda ratio of 31.4 roughly unchanged from the week prior. Repeat immunoglobulin levels and serum protein electrophoresis revealed immune paresis with a stable M spike in the gamma region consistent with known IgG kappa band and stable from prior.

Point of care ultrasound including focused cardiac, lung, and bilateral kidney ultrasound was undertaken. Lung included diffuse A-line pattern in all visualized fields and no pleural effusions (Video S1). Focused cardiac assessment revealed a normal-sized inferior vena cava that collapsed less than 50% with inspiration (Video S2). The right internal jugular vein was undistended 2 centimeters above the sternal angle with the patient in the supine position. (Video S3). Kidney ultrasound revealed enlarged kidneys bilaterally with bilateral hydronephrosis. (Video S4-6 and Figure 1-4).

On ultrasound, hydronephrosis appears as confluent anechoic areas representing urine in a dilated renal pelvis and calyces [1]. In mild hydronephrosis, the renal pelvis and calyces are dilated but the cortex and pelvicalyceal pattern is unaffected. As the hydronephrosis increases in severity, the medullary pyramids flatten and the pelvicalyceal system dilates leading to outpouching of the calyces. In severe hydronephrosis, the renal pelvis may appear ballooned and the cortico-medullary differentiation is lost leading to a thin cortex [2].

On review of the patient's prior imaging, he was noted to have retroperitoneal extramedullary plasmacytomas on a computed tomography scan done six weeks prior. He had interval increase of the plasmacytomas despite initiation of chemotherapy leading to obstruction. Despite the temporal association between our patient starting chemotherapy and the development of acute kidney injury, it was not in fact a causal relationship. The use of POCUS revealed bilateral hydronephrosis and guided our management. We recommended bilateral percutaneous nephrostomy (PCN) insertion as both a diagnostic and therapeutic maneuver. Within 12 hours of PCN placement, his Cr started to decline and within 72 hours his renal function returned to his prior baseline. Ultimately repeat computed tomography demonstrated interval increase in size of retroperitoneal extramedullary plasmacytomas (Figure 5, 6).

When evaluating acute kidney injury (AKI) in multiple myeloma patients the differential diagnosis is wide. Most commonly, myeloma cast nephropathy is suspected. Other causes include deposition diseases, proximal tubulopathy, or direct nephrotoxicity from the various

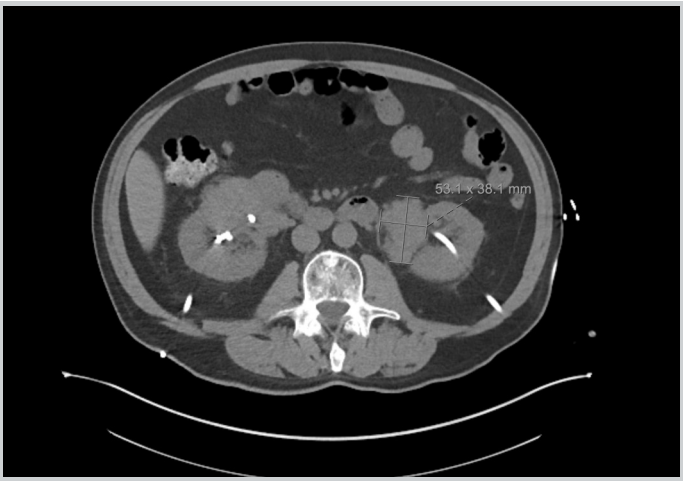

Figure 5. Computed tomography, coronal view in the abdomen demonstrating interval placement of bilateral percutaneous nephrostomies. On the left the plasmacytomas measure 5.3 cm in maximum diameter.

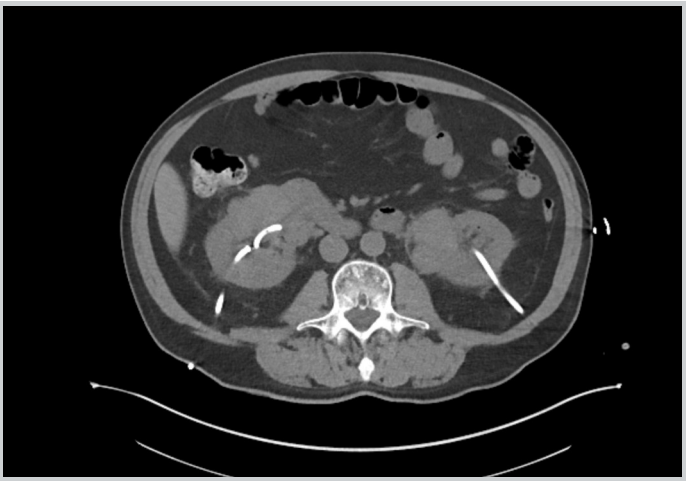

Figure 6. Computed tomography, coronal view in the abdomen demonstrating bilateral kidneys with nephrostomies in place and bulky plasmacytomas at inferomedial border of kidneys bilaterally.

chemotherapeutic and immunotherapy agents used [3]. Acute kidney injury may also arise from side effects of the chemotherapeutic agents which often include nausea, vomiting, and decreased oral intake leading to pre-renal insults or even acute tubular necrosis. Given the bland nature of the urine sediment and lack of physical exam or ultrasonographic evidence of extremes of volume overload our initial differential diagnosis included myeloma cast nephropathy, obstructive nephropathy, and thrombotic microangiopathy due to carfilzomib therapy.

Extramedullary plasmacytomas rarely occur during the course of multiple myeloma with an incidence rate of around 4% [4]. When present, they are most frequently seen along the respiratory tract, lymph nodes and skin and soft tissue. Involvement of the urinary tract is quite uncommon with seven cases involving the renal parenchyma and only two cases of urinary tract obstruction reported in the literature [5, 6]. When evaluating acute kidney injury, a wide differential should be sought, and obstructive nephropathy should be considered. As POCUS is inexpensive and readily available, it should be used in the evaluation of AKI as prompt intervention can lead to marked improvement and even resolution of kidney injury.

Patient Consent

The authors certify that informed consent was obtained for the clinical information and images reported.

Disclosures

None.

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Case Report

Recovery of Severe Acute Kidney Injury in a Patient with COVID-19: Role of Lung Ultrasonography

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Abstract

Acute kidney injury (AKI) is recognized as a complication of COVID-19 among hospitalized patients. Lung ultrasonography (LUS) can be a useful tool in the management of COVID-19 pneumonia when interpreted correctly. However, the role of LUS in management of severe AKI in the setting of COVID-19 remains to be defined. We report a 61-year-old male who was hospitalized with acute respiratory failure from COVID-19 pneumonia. In addition to requiring invasive mechanical ventilation, our patient developed AKI and severe hyperkalemia requiring urgent dialytic therapy during his hospital stay. Our patient remained dialysis dependent despite subsequent recovery of lung function. Three days following discontinuation of mechanical ventilation, our patient developed a hypotensive episode during his maintenance hemodialysis treatment. A point of care LUS performed soon after the intradialytic hypotensive episode found no extravascular lung water. Hemodialysis was discontinued and the patient was initiated on intravenous fluids for one week. AKI subsequently resolved. We consider LUS an important tool in identifying COVID-19 patients that would benefit from intravenous fluids following recovery of lung function.

Introduction

COVID-19, the disease caused by SARS-CoV-2, is commonly associated with acute respiratory failure among hospitalized patients [1]. Acute kidney injury (AKI) has also been reported in a significant percentage of hospitalized patients with COVID-19, many of whom have required dialysis. A restrictive fluid balance in patients with acute lung injury is associated with fewer days of invasive mechanical ventilation [2]. As a result, many physicians employ a strategy of keeping lungs “dry” through diuretics, and when necessary, ultrafiltration.

Lung ultrasonography (LUS) is a useful tool for evaluating pulmonary disease [3,4]. A recent Italian study reviewed the importance of LUS in management of patients with COVID-19 pneumonia [5]. Here, we describe a case wherein LUS provided critical information to successfully treat AKI in a patient recovering from COVID-19 pneumonia.

Case Presentation

A 61-year-old male with no significant past medical history was hospitalized with COVID-19 at our tertiary care facility in Queens, New York in early April 2020. The patient presented with two weeks of intermittent fevers at home and was tested positive for COVID-19 prior to hospitalization. On presentation, the patient’s body temperature was 103°F, blood pressure (BP) was elevated at 184/90 mmHg, heart rate was 110 bpm, body weight was 100 kg, and pulse oxygen saturation was significantly low at 74% on non-rebreather O2 mask. Blood work showed blood urea nitrogen of 15 mg/dL and serum creatinine of 0.97 mg/dL. Arterial blood gas was significant for pH 7.13, $PaCO_2$ 80 mmHg, measured HCO_3 23 mmol/L. Chest x-ray showed bilateral opacities. The patient was emergently intubated and placed on mechanical ventilation on hospital day 1.

On hospital day 2, the patient was noted to have AKI with severe hyperkalemia and persistent acidosis. Blood urea nitrogen was 24 mg/dL, serum creatinine increased to 1.49 mg/dL, serum potassium was significantly elevated at 7.9 mEq/L, and pH remained low at 7.1. Nephrology was consulted and continuous veno-venous hemodiafiltration (CVVHDF) was urgently initiated. On hospital day 7, the patient was transitioned from CVVHDF to intermittent hemodialysis (IHD). The patient was oliguric from hospital day 2 to 11. He was successfully extubated on hospital day 14. On hospital day 17, blood urea nitrogen and serum creatinine remained significantly elevated at 198 mg/dL and 7.88 mg/dL, respectively. On the same day, the patient became hypotensive during his IHD treatment. At the start of IHD treatment, the patient’s BP was 146/94 mmHg and after 50 minutes of dialysis, BP decreased to 76/59 mmHg. He was not requiring supplemental oxygen at that time but was subjectively dyspneic and tachypneic to 30 breaths per minute.

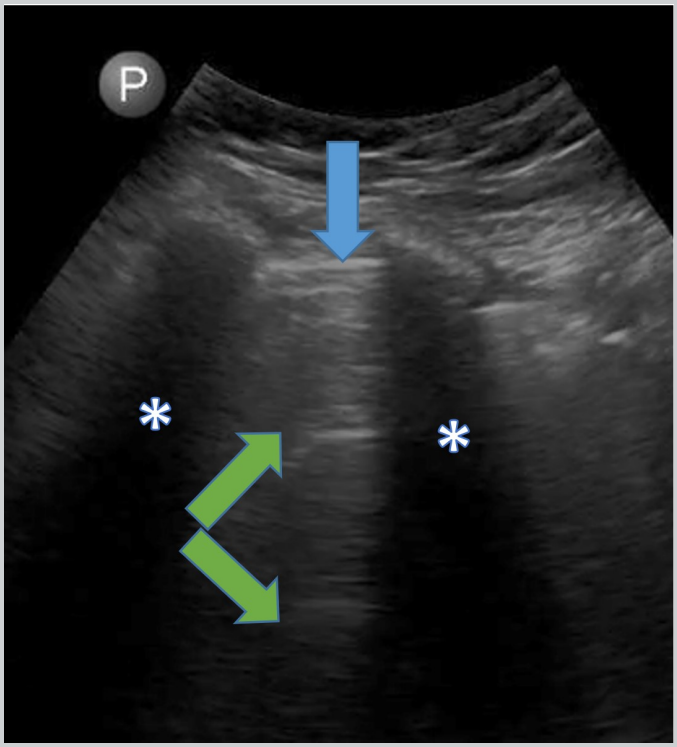

Figure 1. Lung ultrasound image obtained using a curvilinear probe. Blue arrow shows the pleural line, Green arrows show A-lines. Asterisks indicate rib shadows.

An 8 zone lung ultrasound was performed at bedside soon after the hypotensive episode. Findings demonstrated predominantly A-lines with intact lung sliding (Figure 1). The patient's obese body habitus and the availability of only a curvilinear ultrasound probe precluded us from performing a point of care echocardiogram. Following LUS the patient was initiated on intravenous saline infusion and further dialytic therapy was discontinued. After seven days of continous saline, blood urea nitrogen improved to 56 mg/dL and serum creatinine decreased to 1.99 mg/dL. After a month of hospitalization, serum creatinine further improved to 1.00 mg/dL at discharge.

Discussion

Our patient had acute respiratory distress syndrome (ARDS) from COVID-19 pneumonia. Hospital course was complicated by oliguric AKI, severe hyperkalemia, and acidosis requiring initiation of dialytic therapy. During the initial part of his hospitalization, dialytic therapy played a key role in oxygenating and ventilating our patient. Our patient remained dialysis dependent despite resolving respiratory failure. Three days following extubation, the patient developed an episode of intradialytic hypotension. LUS was performed for realtime evaluation of his lung disease. His lung ultrasound findings revealed a normal aeration pattern suggesting low level of extravascular lung water and possibly a pre-renal state.

Air is a poor conductor of sound. When an ultrasound wave passes from the pleural surface to the underlying air the mismatch in acoustic impedance sends a strong echo back to the interface between the skin and the probe. When the echo meets this second strong reflector (the skin-probe) it is reverberated back again to the pleural line. This reverberation is misinterpreted by the ultrasound software and appears as a linear structure deep to the pleural line. These artifacts are known as A-lines and are consistent with a normal aeration pattern. In their seminal work, Lichtenstein et al. have demonstrated that A-lines are strongly predictive of a low pulmonary capillary wedge pressure (PCWP) [4]. When an ultrasound wave meets a water-thickened interlobular septa in the lung, a B-line reverberation artifact is seen. This appears as a straight line that is perpendicular to the pleura and moves as the lung slides. B-line pattern is when three or more B lines are seen at two rib interspaces, bilaterally. B-line pattern can indicate cardiogenic pulmonary edema when the B lines are associated with a smooth pleural line and are distributed homogenously in an interspace. B-lines can also be seen in COVID-19 pneumonia and in the resultant ARDS but typically have an irregular or fractured pleura with sub-pleural consolidations. These findings typically resolve to A-lines with clinical improvement [6].

Our patient was obese and recovering from COVID-19 pneumonia with ARDS. He was dyspneic and tachypneic. His volume status was very difficult to ascertain due to his body habitus. We were concerned that excessive fluid resuscitation could worsen his respiratory status if he was still exhibiting signs of ARDS. In our patient, the presence of A-lines and absence of B-line pattern argued in favor of a resolved COVID-19 pneumonia and ARDS and in favor of a normal or low PCWP. These findings gave us the reassurance to attempt a trial of fluid hydration.

Lung ultrasonography should not be performed in isolation. Ideally, a point of care echocardiogram would have been done as well. Unfortunately, we only had a curvilinear probe at our disposal at the time. Curvilinear probes can be used to image the inferior vena cava (IVC). The patient's body habitus prevented an adequate window to view the IVC. Intradialytic hypotension can also be caused by pericardial effusion and pulmonary embolism. A limited echo in this case would have been valuable to look for effusion, right ventricular strain, and cardiac contractility. Of note, a referral echocardiogram with contrast was done a few days later. The study was technically limited but ruled out pericardial effusion.

A restrictive fluid approach is commonly used in patients with acute lung injury. This strategy, while crucial for helping with oxygenation, can also lead to pre-renal AKI. Lung ultrasonography is a reliable tool to get real-time, point of care information about a patient's pulmonary status. Based on our experince, LUS may be an important tool in identifying COVID-19 patients that would benefit from intravenous fluids following recovery of lung function.

Conflicts of Interest and Funding

The authors have no conflicts of interest or funding to report.

Acknowledgements

We acknowledge the Northwell COVID-19 research consortium. The initial characteristics of 5,700 patients from Northwell are presented in reference 1 and this case describes one of those patients in-depth.

Informed Consent

The Northwell Health Institutional Review Board approved this case as minimal-risk research using data collected for routine clinical practice and waived the requirement for informed consent however verbal consent was obtained from the next of kin.

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Incidentalomas Among Healthy Nephrology Fellow Volunteers at POCUS Workshops: A Case Series

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Introduction

A radiographic incidental finding (sometimes called an *incidentaloma*) is defined as a structure that is unintentionally found during an exam for an unrelated indication. The increased use of routine abdominal imaging is associated with a rising incidence in incidentalomas of the kidney [1]. In one meta-analysis, 75% of renal incidentalomas were benign [2]. However, the overall prevalence of incidental carcinomas is low at 0.2% [3]. With the growing uptake of POCUS, healthy volunteers for clinical demonstrations may find themselves with new findings despite a lack of symptoms [4]. Having an incidentaloma discovered during the course of a nephrology POCUS workshop is a unique experience. Herein we report our experiences of having incidentalomas discovered during the course of POCUS demonstrations.

Case 1

A 31-year-old male nephrology fellow with history of intraocular hypertension controlled on latanoprost volunteered to serve as a model during a POCUS workshop as part of nephrology fellowship. He first learned the overall technique on an ultrasound simulator and proceeded to self-scan to obtain more practice. Standardized patients were not used due to group restrictions related to the SARS-CoV-2 pandemic. During the course of the examination, he identified a 5 cm anechoic structure with posterior acoustic enhancement at the inferior pole of his right kidney. The anechoic structure was well-circumscribed, thin-walled, and homogenous—lacking in internal echoes. The fellow asked for help from the attending nephrologist who also identified the structure as a simple cyst and ordered a referral study for follow up. A referral ultrasound study confirmed a 5 cm simple cyst at the inferior pole of the right kidney (Figure 1, 2). Serum creatinine was previously normal at 1.0 mg/dL. The fellow's reaction was one of increased confidence in correctly identifying the structure, but a lurking feeling of unease that ethical issues should be considered in using volunteers for such programs.

Renal cysts are a very common finding on ultrasound occurring in more than 1 in 10 patients. Simple renal cysts appear as thin-walled anechoic structures with posterior acoustic enhancement. Simple cysts are benign, but increasing cyst complexity can be categorized according to the Bosniak Classification System with

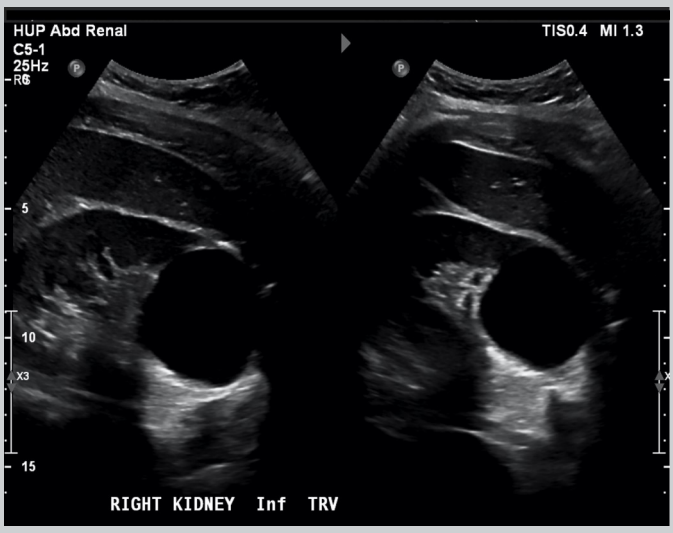

Figure 1. B mode sagittal (left) and transverse (right) imaging planes of right kidney from case 1. Note the thin-walled, anechoic 5 cm simple cyst at the inferior pole of the kidney with posterior acoustic enhancement.

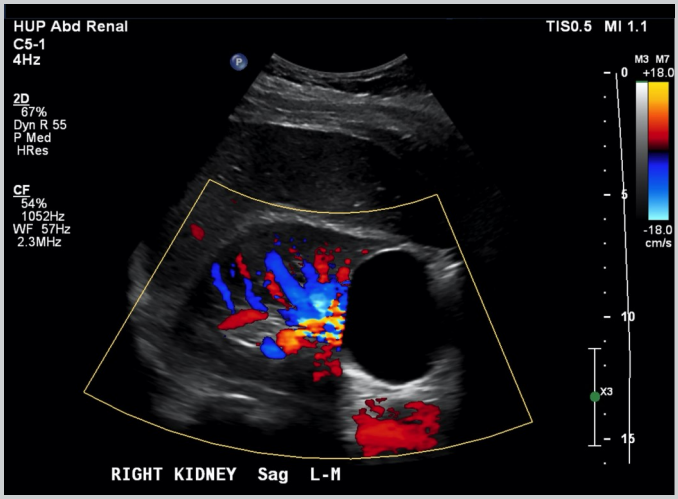

Figure 2. Doppler mode sagittal imaging plane of right kidney from case 1 demonstrating patent renal vasculature and absence of flow within the cyst.

features such as septae, calcifications, vascularity, or solid components associated with increased risk of malignancy [5].

Case 2

A healthy 32-year-old male nephrology fellow volunteered to serve as a model demonstrating renal imaging for a class of undergraduate medical students. The sonographer correctly identified the right renal fossa and liver but could not identify the right kidney. The sonographer quickly moved on to the left side and demonstrated a normal left kidney. The absence of right kidney was communicated to the experienced attending nephrologist and the class of medical students. The attending nephrologist sent the nephrology fellow for a referral study which again demonstrated an empty right renal fossa (Figure 3) and normal left kidney. Ultimately a pelvic kidney was identified in the right iliac fossa with patent vasculature and present right ureteral jet (Figure 4, 5). Serum creatinine was noted to be at the high end of normal at 1.3 mg/dL. The fellow later recalled that he had episodes of gross hematuria as a child following participation in sports. His overall reaction to the episode was bemusement and interest in the embryologic processes that led to this aberrantly placed kidney.

Figure 3. Sagittal imaging plane of right kidney fossa from case 2 demonstrating liver, but no kidney present.

Pelvic kidneys occur in approximately 1 in 500 births and result from the failure of the ascent of the kidney from its embryological origin during the 9th week. Pelvic kidneys are generally asymptomatic and are typically only discovered incidentally, but can be associated with other genitourinary malformations or complications such as obstructing nephrolithiasis. [6].

Figure 4. Oblique imaging plane of right iliac fossa from case 2 demonstrating the presence of renal parenchyma in this ectopic location.

Case 3

A healthy 33-year-old male nephrology fellow scanned his own kidneys and bladder to generate normal images for a seminar on kidney and bladder ultrasound for nephrology fellows and attendings. He discovered a junctional parenchymal defect on his right kidney which he recognized by its distinctive appearance from a prior kidney ultrasound seminar (Figure 6). The kidneys and bladder were otherwise without abnormalities. A serum creatinine had been normal at 1.0 mg/dL on routine blood work one year prior. Referral imaging confirmed the finding of junctional parenchymal defect. He included the gathered images in the lecture as planned and later included the finding in a case series on incidental findings. His overall reaction was one of pleasure and self-satisfaction for correctly identifying the anatomical variant and at the opportunity to publish the finding in a peer-reviewed journal.

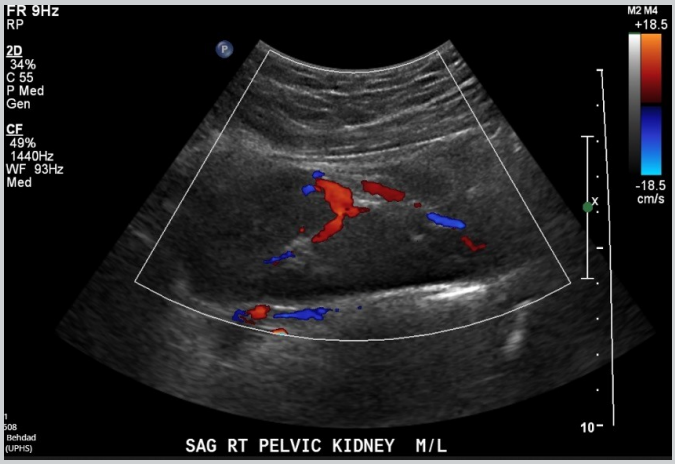

Figure 5. Doppler mode oblique imaging plane of right iliac fossa from case 2 demonstrating the presence of patent renal vasculature within the renal parenchyma in this ectopic location.

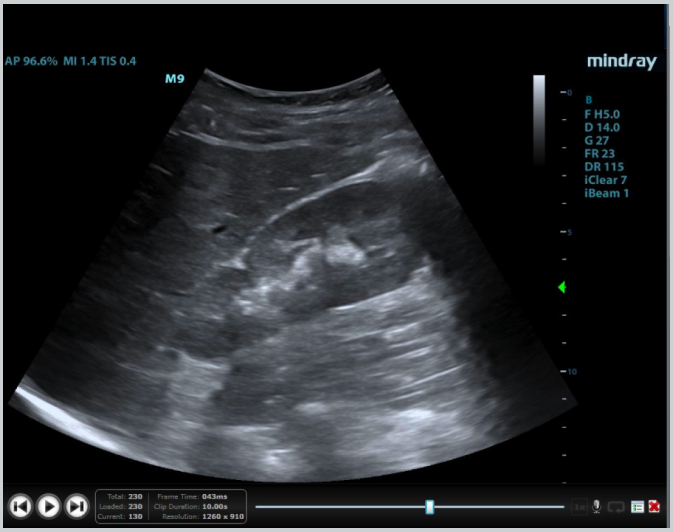

Figure 6. B mode sagittal imaging plane of right kidney demonstrating junctional parenchymal defect with characteristic “shark’s tooth” appearance. Note overlying liver isoechoic to kidney cortex.

A junctional parenchymal defect (JPD) is a triangular area hyperechoic to the renal parenchyma that can be mistaken for scar or mass. JPDs are most commonly seen in the upper pole of the right kidney representing an extension of the sinus fat and embryologically arising from fusion of embryologic renal precursors. Continuity of the JPD with renal sinus fat differentiates them from other pathologic lesions [7].

Discussion

We reported three incidentalomas occurring in healthy nephrology fellows volunteering for POCUS workshops. In all three cases the findings were benign and represented the typical spectrum of findings on kidney ultrasound. This case series is limited in scope due to the small number of patients and demographic homogeneity. Loss of confidentiality in the case of an incidentally discovered finding remains a concern. Given these concerns we implemented a protocol faculty similar to that put forth by Siegel-Richman and Kendall [4]. Namely, volunteers, whether students or standardized patients, have the right to have such incidental findings remain confidential, as well as the option to either pursue or refuse further diagnostic testing. Instructors and sonographers, for their part, should respect the wishes of the participants but remain vigilant and, regardless of their insurance status, recommend further testing and, if indicated, medical attention without delay.

Statement of ethics approval/consent

Authors state that they have no conflicts of interest. Authors attest that they give their consent for reproduction of the included images.

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Case Report

Point of Care Ultrasound in Monitoring of Post-Renal Biopsy Bleeding

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Abstract

A 32-year-old male presented with hypertensive emergency and features of thrombotic microangiopathy. He underwent a kidney biopsy after renal dysfunction persisted despite clinical improvement otherwise. The kidney biopsy was performed with direct ultrasound guidance. The procedure was complicated by hematoma formation and persistent turbulent flow on color Doppler concerning for ongoing bleeding. Serial point of care ultrasounds of the kidney with color flow Doppler were used to monitor the size of the hematoma and determine if there was evidence of ongoing bleeding. These serial ultrasounds showed stable hematoma size, resolution of biopsy-associated Doppler signal and prevented further invasive interventions.

Case Report

A 32-year-old male with type 1 diabetes mellitus presented to the emergency department with altered mental status, hypertensive emergency, microangiopathic hemolytic anemia (MAHA), and acute kidney injury (AKI). Brain imaging showed diffuse edema of the pons and medullary pyramids concerning for atypical posterior reversible encephalopathy syndrome (PRES). He was admitted to the ICU for hypertension control and further monitoring. He was presumed to have a thrombotic microangiopathy (TMA) in the setting of malignant hypertension, but despite improvements in his mental status and stabilization of his AKI with intensive blood pressure control he had evidence of persistent MAHA with ongoing schistocytosis. A kidney biopsy was pursued to determine if additional tissue characteristics would identify alternative cause of his presumed TMA.

A left kidney biopsy was performed using a 16-gauge biopsy needle with direct ultrasound guidance. The biopsy was performed by clinical nephrology faculty and nephrology fellow. The biopsy was performed in the patient's hospital floor room in a unit designated for renal biopsies. Three passes were performed. After the third pass, a post-procedural hematoma and tract of turbulent flow on color Doppler was noted at the lower pole of the left kidney concerning for ongoing bleeding (Figure 1). Pressure was held and the site was monitored for 30 minutes. Between 15 minutes and 30 minutes post-procedure, the size of the hematoma was unchanged and the flow on color Doppler decreased. He remained normotensive and pain was minimal. Given the stable hematoma size on ultrasound and reassuring clinical parameters, a plan for serial ultrasounds throughout the afternoon was made. Repeat renal ultrasound was performed 90 minutes after the procedure which showed

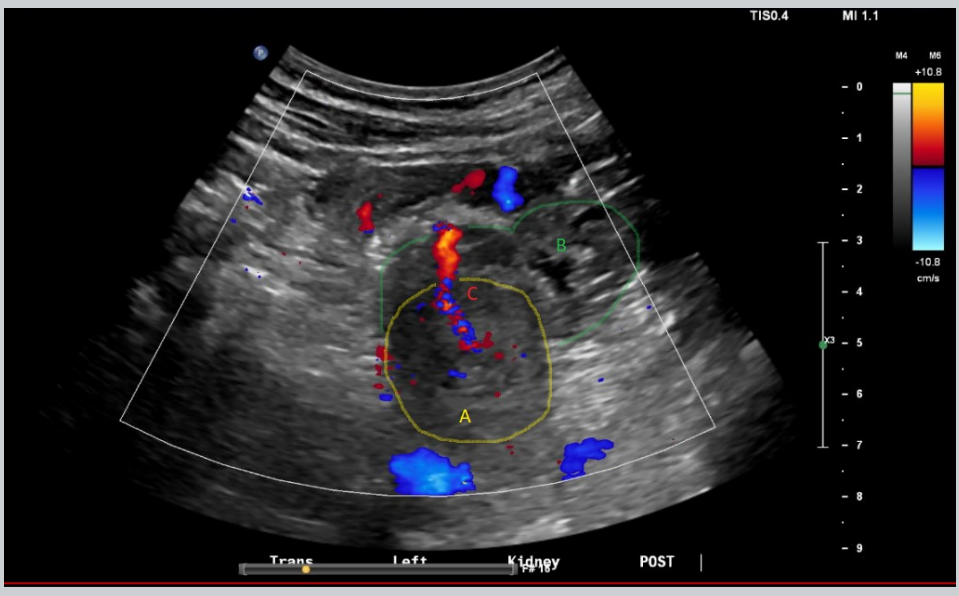

Figure 1. (A) Left kidney, lower pole; (B) hematoma; (C) Doppler flow signal from vascular jet. Initial ultrasound showing persistent bleeding evidenced by ongoing tract of turbulent flow on color Doppler. Hematoma size 7.8 x 1.8 x 4.7cm.

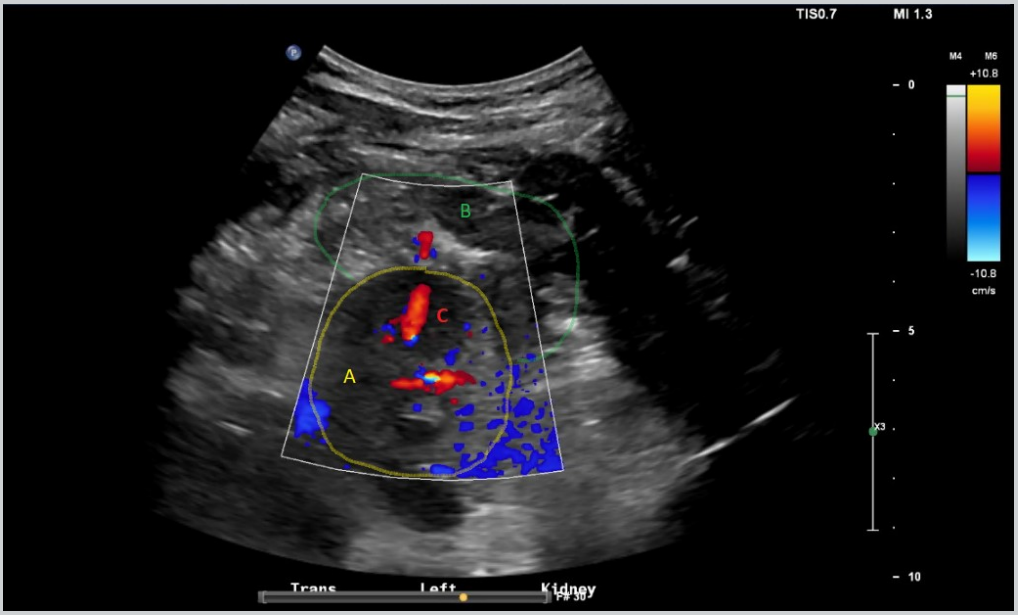

Figure 2. (A) Left kidney, lower pole; (B) hematoma; (C) Doppler flow signal from vascular jet. Ultrasound at 90 minutes after biopsy. Persistent bleeding evidenced by ongoing tract of turbulent flow on color Doppler. Hematoma size 7.9 x 2.3 x 4.9cm.

persistent tract of flow on Doppler but similar hematoma size. The Doppler signal was also less intense (Figure 2). A third ultrasound, performed 4 hours after initial procedure, demonstrated stable hematoma size and no further evidence of Doppler signal suggesting no ongoing active extravasation. The follow-up ultrasounds were performed by a radiology ultrasound technician with the nephrology attending in observation and involved in clinical decision making in real time. Referral ultrasound images were additionally read by a radiologist.

He was monitored closely overnight as per standard hospital post-kidney biopsy protocols. His hematocrit was checked every 4 hours and remained stable. Results of the biopsy indicated severe diabetic nephropathy, accelerated hypertension related injury but no evidence of TMA. He was discharged the following day. At his clinic follow-up 2 weeks after discharge, his hematocrit was stable and he had no further evidence of complications from kidney biopsy.

The most common complication of kidney biopsies is bleeding [1, 2]. Hematomas are reported in up to 57% to 91% of native kidney biopsies by CT and have been reported up to 86% of cases by ultrasound [1, 3]. Most commonly, hematomas are clinically silent and do not require additional intervention (4, 5). In patients who do have clinically significant complications, hematomas are noted by 1 hour post biopsy in 77% of cases and were measured at >3cm in greater than 50% of cases [3]. Presence of a color tract on doppler has also been shown to be 10.7 times more likely to result in major and minor complications [6].

Major bleeding complications include need for transfusion, need for secondary procedures to stop arterial bleeding, and death. These complications occur in up to 2% of native kidney biopsies with 1.6% (1 in 625) requiring transfusion, 0.3% (1 in 333) requiring secondary intervention to stop arterial bleeding after biopsy, and 0.008% (1 in 12,500) resulting in death [2]. At our institution, our first line therapy for secondary intervention is an arteriogram with dedicated coil and or embolization.

In this case, the size of the hematoma and velocity of the Doppler signal at the end of the procedure were concerning and suggested that the patient may require a secondary intervention to halt the bleeding. POCUS allowed us to monitor hematoma size and the velocity of the Doppler signal of the bleeding in real time. Serial monitoring with POCUS enabled demonstrable cessation of bleeding, stability of the hematoma in size, and deferral of any emergent secondary intervention with angiogram or embolization.

Disclosures

None

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Review

Ultrasonography in Acute Kidney Injury

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Introduction

Advances in the use of ultrasonography can enhance our ability to better characterize acute kidney injury (AKI). AKI is a clinical syndrome characterized by a rapid decrease in kidney excretory function with the accumulation of products of nitrogen metabolism and other clinically unmeasured waste products, and may proceed to include clinical manifestations including decreased urine output, development of metabolic acidosis, and electrolyte abnormalities [1]. The Kidney Disease Improving Global Outcomes (KDIGO) criteria defines AKI (Table 1). Staging severity of AKI guides the physician in respect to medical management and prognosis. The overall incidence of AKI is around 20% of patients hospitalized worldwide, and around 50% in intensive care unit (ICU) patients [2, 3]. AKI has been found to have increasing morbidity and mortality, no matter the cause of admission, as well as an in-hospital mortality of close to 50% [4]. In a large study of 8 ICUs over 8 years, Kellum et al. found that AKI was associated with increasing mortality rate with worsening AKI stage. A decrease in urine output alone, without an increase in serum creatinine, was associated with decreased 1-year survival [5]. Recurrent AKI has also been associated with increased mortality, further demonstrating the importance of detecting, monitoring, and diagnosing AKI [6].

An approach to AKI differentiates between pre-renal, intrinsic, and post-renal/obstructive AKI. Pre-renal AKI results from decreased perfusion of the kidney parenchyma. Intrinsic AKI is an insult that progresses to damage of the kidney tubules and/or direct damage to the nephron itself. Post-renal AKI develops from an obstruction of urine downstream of the kidney collecting system, such as in nephrolithiasis, a malignancy compressing a ureter, or in prostatic hypertrophy. Pre-renal and post-renal injuries are typically reversible, but prolonged injury may develop into intrinsic AKI. The rapid diagnosis of pre- and post-renal obstruction can lead to reversal. Ultrasonography through high quality imaging is therefore critical for clinical care [7]. Kidney ultrasonography is usually performed by trained ultrasound technicians with a radiologist interpretation. Point of care ultrasound, when wielded by a clinician, can aid in rapid evaluation of AKI. In this review we will examine the evolving role of kidney ultrasound in AKI management.

Kidney Imaging

Kidney length norms were established by Emamian et al. who studied 665 healthy volunteers of various ages to establish median kidney lengths of 11.2 cm on the left and 10.9 on the right side [8]. Kidney length correlates linearly with patient height, and so should be taken into account when determining expected kidney length [8]. When performing kidney ultrasonography, taking the time to obtain multiple kidney images can assist in obtaining accurate measurements. In addition, be aware that congenital abnormalities of the kidney and urinary tract (CAKUT) have a prevalence of three and six per 1,000 live births [9, 10]. Solitary kidney/unilateral kidney agenesis occurs in 1 in 1000 live births, more frequently in women and more often on the left [11]. These patients have an increased risk of CKD progression [12]. Duplicated collecting systems can also be observed in the absence of history of urinary tract infections and should be differentiated from hydronephrosis. Bladder imaging is important when performing kidney ultrasonography to identify the site of outflow obstruction.

Table 1. Stages of AKI as defined by KDIGO. (Adapted from [1].)

Stage of AKI	Serum Creatinine	Urine output
1	1.5-1.9 times baseline OR ≥0.3 mg/dL	<0.5mL/kg/h for 6-12 hours
2	2.0-2.9 times baseline	<0.5mL/kg/h for ≥12 hours
3	3.0 times baseline OR Increase in serum creatinine to ≥4.0 mg/dL OR initiation of kidney replacement therapy OR in patients < 18 years, decrease in GFR to <35 mL/min per 1.73 m^2	<0.3 mL/kg/h for ≥24 hours OR Anuria for ≥12 hours

Figure 1. Normal kidney on ultrasound. Sagittal view of normal left and right kidney. Note the isoechoic nature of the cortex with the liver and spleen with hyperechoic sinus fat in the center. The hypoechoic medullary pyramids surround the sinus fat. *Image from Koratala, A. POCUS Gallery. Renal Fellow Network. Accessed November 27, 2020. https://www.renalfellow.org/pocus-gallery/ Used with Permission*

Figure 2. Moderate hydronephrosis. The usually hyperechoic sinus is pushed and thinned as the pelvis swells with hypoechoic urine, making the center of the kidney dark. Note the connection with the ureter, confirming that it is the urinary tract swelling and not parapelvic cysts. *Image courtesy of Abhilash Koratala. renalfellow.org/pocus-gallery. Used with permission*.

Ultrasonography can also assist in distinguishing AKI from chronic kidney disease (CKD). Often in CKD, the kidney length decreases, and severe CKD can be characterized by a combined kidney length of <20 cm [13]. Changes in kidney size can also be indicators of other types of chronic disease. Enlargements in kidney size can be associated with deposition-type diseases, most notably amyloidosis, diabetes, lymphomatous invasion, and HIV [13-16]. In patients with amyloidosis and lymphoma with established kidney disease, changes in size help monitor the progression of disease or treatment response. Early in the progress of these diseases, there is deposition and swelling, but afterward, the kidney shrinks as in other progressive causes of CKD (Figure 1, Figure 2).

Cortical thickness is another measurement to help distinguish CKD from AKI. Cortical thickness is measured on a longitudinal ultrasound image of the kidney, perpendicularly from the outer margin of the kidney to the corticomedullary junction. In a study by Beland et al. of 25 patients not on dialysis, the cortical thickness was shown to be more closely related to the estimated glomerular filtration rate (eGFR) than the kidney length. The normal thickness is between 8 and 10mm, Cortical thickness worsens in a stepwise progression with decreases in kidney function [17, 18]. Cortical thickness also has excellent interobserver correlation, which makes it well suited for management and monitoring of kidney function over time [18, 19].

Another characteristic of CKD is the degree of echogenicity. The echogenicity is the brightness of the cortex on ultrasound compared to the liver, assuming normal liver function. The kidney is normally isoechoic or hypoechoic to the normal liver or spleen (Figure 3B). One must have caution when making this comparison in patients with liver disease, as especially fatty liver disease or fibrosis can increase the echogenicity of the liver, making the comparison more difficult.

The echogenicity of the kidney is increased in disease states that increase fibrous tissue such as CKD. Inflammatory infiltrates from acute interstitial nephritis

Table 2. Summary of ultrasound findings in kidney insufficiency.

Kidney Insufficiency	Ultrasound Findings	Pearls and Pitfalls	Next steps
CKD	Decreased kidney length [8], decreased cortical thickness [17], [18], Increased echogenicity [13]	Increased echogenicity is subjective and can be skewed by liver disease. Depending on disease course kidney length can be increased or decreased.	Establish baseline serum creatinine, monitor for change, rule out AIN
Pre-Renal AKI	Decreased vascular exam (low IVC collapsibility index, low ultrasound internal jugular collapse point, collapsible ventricles, and atria), clear lung fields	Mixed pictures are often possible in disease states such as pulmonary hypertension and liver cirrhosis with high total body or lung fluid and low intravascular fluid	Fluid resuscitation, amplification of forward flow with pressors or inotropes, monitoring of creatinine change
Post-Renal AKI	Hydronephrosis, calcified papillae	Non-dilating obstruction also exists, if high suspicion may need functional test or urologic procedure [35-38] Non-pathologic causes of hydro: pregnancy, with high amounts of diuresis, and with congenital nephrogenic diabetes insipidus [30-34]	Relief of obstruction, monitoring of creatinine change, treatment of underlying papillary necrosis
AIN	Increased echogenicity	Multiple causes with varied workup. Echogenicity non-diagnostic	Kidney biopsy, serologic markers, monitor echogenicity and size for improvement with treatment
DM	Increased size, then decreased size with sclerosis	Normal kidney size can be an indication of entering sclerosing phase	Aggressive treatment and monitoring of DM
ATN	Decreased mobility with respiration, enlargement, thickened capsule, ±corticomedullary differentiation [45]	Early ATN: increased corticomedullary differentiation. Late/severe ATN: decrease corticomedullary differentiation [30, 45]	Treat the underlying cause, monitor anteroposterior to longitudinal diameter ratio: increased having a worse prognosis [46, 47]
Infiltrative disease	Multiple myeloma: hyperechoic, no change in size [48] Lymphoma: hypoechoic, and diffusely enlarged [49] Amyloid: hyperechoic, enlarged early then small	Differentiate lymphomatous invasion from xanthogranulomatous pyelonephritis	Kidney biopsy, serologies, monitor size and echogenicity for treatment response
Venous Congestion	Systolic reversal of hepatic venous flow, severe portal flow pulsatility, severe alteration in intra-renal venous flow, and expanded IVC with low collapsibility index. High ultrasound collapse point on internal jugular vein	Many alterations in intraabdominal pressure (ascites, surgical abdomen), intrathoracic pressure (Intubation, pulmonary hypertension) can affect the individual measurements and should be taken as a whole	Diuresis, serial monitoring of vascular findings to confirm improvement with fluid removal
Renal vein thrombosis	Sparse arterial and venous flows, reverse diastolic flows, increased resistive index [64]	Important in the context of nephrotic syndrome	Anticoagulation, consider invasive treatment
Hemorrhagic infarct	Hypoechoic free area, swollen parenchyma, lack of arterial flow to the area	Almost always secondary to cardiac disease as a source of embolism	Treatment of underlying disease
Cortical Necrosis	Hypoechogenic cortex	Only seen in severe ischemic states	Treatment of underlying shock, poor prognosis

Figure 3. Increased Echogenicity. A) Right kidney long axis, hyperechoic cortex compared to liver, however cortex has normal thickness and length normal for size. Patient found to have positive serologies and proliferative lupus nephritis. B) Right kidney, long axis. Patient with advanced chronic kidney disease. Note the hyperechoic renal cortex and thin parenchyma with both cortex and medulla <1cm. C) Left kidney of patient with ATN, biopsy proven, from myoglobinuric kidney injury. Note the increased echogenicity of the cortex with increased differentiation of the medulla and cortex. *Images courtesy of Abhilash Koratala Nephropocus.com Used with permission*.

(AIN) or glomerulonephritis (GN) can also increase echogenicity due to inflammatory infiltrates, as will be discussed later. The amount of echogenicity correlates well with the severity of kidney disease and, when combined with decreased length, is specific for severe chronic kidney disease [13]. A summary of etiologies of kidney dysfunction and their ultrasound findings are summarized in Table 2.

AKI - Ultrasonographic Assessment

Pre-renal AKI

AKI due to pre-renal etiologies requires the assessment of volume status in addition to metabolic and urinary data. The use of ultrasound in volume assessment is discussed in detail in this issue on POCUS, therefore will be reviewed briefly here. The volume state of patients is often difficult to assess in patients with extravasation of fluid due to cancer or liver disease or due to body habitus and so the true intravascular volume is unknown. Ultrasound of the inferior vena cava (IVC) and internal jugular vein can help to distinguish between fluid overload and volume depleted states [20-22]. These measurements have improved interobserver reproducibility over jugular venous distension alone, and when combined have excellent correlation with the central venous pressure (CVP), especially when the volume status is low [21, 22]. In this way, a point of care ultrasound can help guide the need for fluids in patients with AKI.

Post-renal AKI

Post-renal obstruction can occur acutely or can be a chronic clinical state. Special populations include children and men with prostate disease. CAKUT incidence in the United States is between 0.3-1.6 in 1000 births, compared to 4.2 per 10,000 births in Taiwan [23-26]. Benign prostatic hypertrophy is a more common entity in the US, with prevalence rates between 50%-75% among men older than 50 and 80% in men over 70 years old [27]. Hydronephrosis is detected in <10% of patients evaluated for AKI, though this rate varies depending on the patient population (Figure 2) [28, 29]. Hydronephrosis is described in non-pathologic physiologic states as well, most notably in pregnancy and congenital nephrogenic diabetes insipidus [30-34]. Cases of non-dilated obstructive uropathy have been reported in patients with malignancy, nephrolithiasis, and post-surgical collections which lead to kidney parenchymal compression and high pressure in Bowman's space mitigating the development of hydronephrosis [35-38]. Of particular importance is to rule out obstruction in patients with malignancy, as obstruction can sometimes be the presenting complaint in progression of disease. Indeed, any part of the urinary tract can be affected by malignancy and should be monitored closely when a history of malignancy is present [39].

Another consideration that contributes to diagnoses of hydronephrosis includes appropriate interpretation of echogenicity of kidney and evaluation of the bladder wall (Figure 4). Visualizing the distal ureter at the ureteropelvic junction and the proximal ureter at the junction with the renal pelvics can provide clues in evaluating the etiology of hydronephrosis. Central sinus fat is normally echogenic. Kidney calyces are not visible unless dilated and hydronephrosis should be differentiated from a kidney sinus cyst which is rounded and has no communication with the collecting system. Stones, masses, and prostatic hypertrophy can often be identified as etiologies of obstruction in those with hydronephrosis. Within the bladder, color Doppler ultrasound can identify ureteral jets which can help distinguish functional (presence of jets) and non-

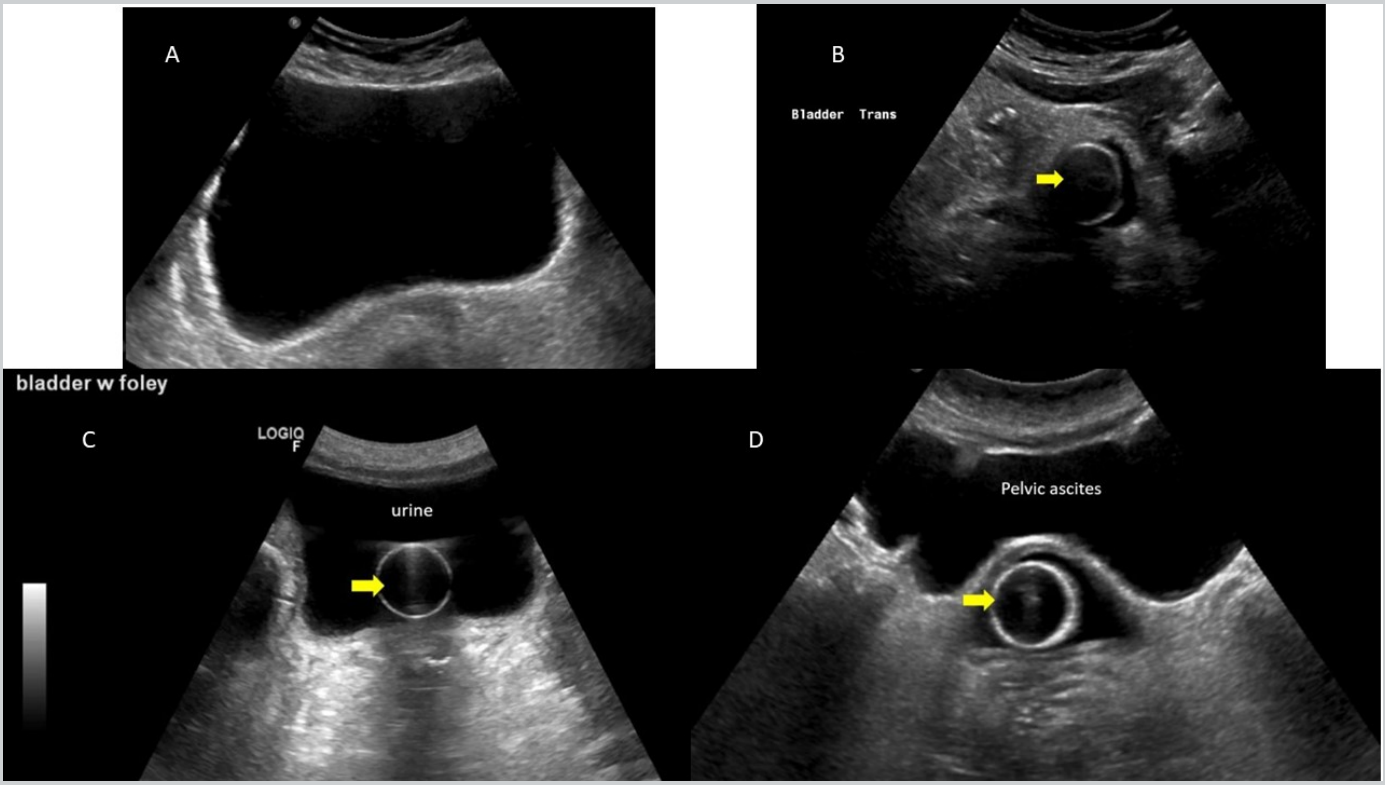

Figure 4. Bladder ultrasound. A) Normal transverse ultrasound of a full bladder. B) Decompressed bladder around an indwelling urinary catheter. Notice a small amount of hypoechoic urine around the catheter which is normal. C) Indwelling urinary catheter within a non-empty bladder. Note there is still a lot of anechoic urine within the bladder. This measured as >200 mL indicating improper drainage of urine. The indwelling urinary catheter was replaced and urinary flow resumed. D) Pelvic ascites mimicking bladder. Ascites is a common false positive for bladder scanners which mistake it for urine. On ultrasound we see the indwelling urinary catheter surrounded by a decompressed bladder (arrow). Superficial to this, one can see pelvic ascites interdigitating among abdominal viscera and tracking into the paracolic gutters. *Images courtesy of Abhilash Koratala. Renalfellow.org/pocus-gallery. Used with permission.*

functional (absence of jets) obstruction [40]. Ultrasound of the indwelling urinary catheter in the bladder ensures appropriate placement.

Papillary necrosis is an interesting cause of hydronephrosis. The necrosed papilla sloughs into the urinary space and fills the ureter at the site of obstruction [41]. Papillary necrosis results due to ischemic changes at the kidney pyramids, which are more vulnerable to ischemia due to low blood flow and a hypertonic environment. This can be related to sickle cell disease, sickle cell trait, analgesic abuse, diabetes, vesicoureteral reflux, or other vasculitic diseases. In cases where the necrosed papillae remain in situ, or with repetitive events such as with sickle cell disease, the papillae can become calcified, which can be readily seen on kidney ultrasound.

Intrinsic AKI

The broadest and most varied cause of AKI has to do with the kidney itself, and ultrasound can offer glimpses into diagnosis and treatment in this case as well. AIN is most readily diagnosed by biopsy, but ultrasound can play a role as well. HIV associated nephropathy has been studied and followed before effective treatment and was found to have increased echogenicity in the acute phase, and the amount of echogenicity and response to treatment correlated well with survival [42, 43]. This has also been applied to lupus nephritis and other causes of AIN to monitor the response to treatment and predict flares. As with other types of kidney disease, later in the time course the echogenicity becomes permanently increased and the size of the kidney is reduced.

Diabetic nephropathy can have characteristic findings on ultrasound. During the early phase of diabetic nephropathy, the kidney is enlarged with a concurrent rise in GFR associated with hyperfiltration [16]. This is seen concurrently with microalbuminuria, and as the disease progresses it will then start to sclerose [44]. In patients with diabetes mellitus and advancing CKD based on eGFR with “normal” kidney size, the kidney size may be misleading as diabetic kidney disease can lead to enlargement of the kidneys. In these patients, this phase of diabetic kidney disease is often rapid and will fit the

definition of AKI, though this actually reflects ongoing CKD progression.

One of the most common causes of AKI in the ICU is acute tubular necrosis (ATN). ATN is caused by a variety of conditions, including the progression of pre-renal and post-renal injuries, sepsis, shock, and both endogenous and exogenous toxins. On ultrasound, there is decreased mobility with respiration, enlargement, and a thickened capsule with impaired corticomedullary differentiation [45]. Early in ATN, the increased echogenicity tends to spare the medullary pyramids, yielding *greater* corticomedullary differentiation (Figure 3C). However, as it progresses or becomes more severe, the medullary pyramids become swollen and echogenic as well due to distal tubule involvement [30, 45]. Monitoring the size of the kidney during ATN can help to prognosticate as well, with increased anteroposterior to longitudinal diameter ratio having a worse prognosis [46, 47].

Infiltrative disease can be readily monitored and assessed on ultrasound as already mentioned. While serologies and biopsy are the mainstays of diagnosis, monitoring and differentiation can be readily assessed with repeated kidney ultrasound. In multiple myeloma, the kidney will appear hyperechoic with no change in kidney size and no change in resistive index (RI) [48]. In lymphoma, the kidney often appears hypoechoic and diffusely enlarged on ultrasound [49]. One should take particular care to differentiate this imaging from xanthogranulomatous pyelonephritis, which should be readily distinguished by the presence of staghorn calculus and pyuria in the latter. Amyloid, like multiple myeloma, will typically demonstrate increased cortical echogenicity on ultrasound, but is differentiated clinically by the presence of albuminuria and nephrotic synrome, rather than paraproteinuria. AA amyloidosis can be associated with chronic inflammation or chronic infections, such as tuberculosis [50]. The amyloid kidney is often enlarged early in the disease course and, like diabetes, becomes smaller with loss of kidney function [15].

Vascular assessment

Point of care ultrasound with Doppler assessment of the abdominal parenchymal vessels has found increasing use in recent years. It is a higher level application of B-mode point of care ultrasound and is discussed separately to differentiate from the general discussion of point of care ultrasound in AKI, but many of the assessments can be used to confirm diagnosis as above.

The resistance index (RI) is defined as the (peak systolic velocity – end-diastolic velocity)/peak systolic velocity of the intrarenal arteries. Normal RI is considered between 0.5-0.7, with elevations associated with higher ICU mortality and persistent AKI [51]. Most parenchymal diseases result in a non-specific elevation, such as obstruction, hepatorenal syndrome, sepsis, and in acute rejection in the transplant allograft. It is normal to decreased in pre-renal azotemia, however, and may be useful in distinguishing pre-renal vs parenchymal disease/ATN when <0.7 [52].

The venous excess ultrasound (VExUS) grading system was developed to help increase the ability to distinguish vascular overload and organ congestion. It is discussed in detail elsewhere, so will be mentioned briefly here. In a post hoc analysis of a single-center prospective study of 145 patients, Beaubien-Souligny et al. created a system to grade the ultrasound findings combining IVC measurement, hepatic vein Doppler, portal vein Doppler, and intra-renal venous Doppler. This combination, used in “VExUS C” grading system outperformed all others including CVP measurement and IVC measurement alone to predict AKI [53]. This finding was in non-critically ill patients undergoing cardiac surgery, and so may not be able to be generalized to other patients. When there is a systolic reversal of hepatic venous flow, severe portal flow pulsatility, severe alteration in intra-renal venous flow, and expanded IVC there is a high likelihood of venous congestion [53, 54].

Nephrotic syndrome is a disease state where vascular ultrasonography for volume status assessment is of particular importance. Patients with nephrotic syndrome are hypercoagulable from several different mechanisms but have been found to have an increased risk of venous thromboembolism, and about 40% of patients develop some form of clot [55]. When these patients develop AKI, it is important to rule out renal vein thrombosis as the cause, as there is a high rate among patients with nephrotic syndrome [56].

The last aspect of the vascular exam in AKI is a consequence of impaired flow, which Doppler ultrasound can confirm. Renal infarction is often embolic and sequelae of cardiac disease as the main source of embolic material. The infarct is an echo-free area, with swollen parenchyma, and Doppler can be used to confirm the lack of flow to the area [57]. This should be contrasted to cortical necrosis, which is a dark hypoechogenic kidney cortex entirely and is secondary to severe ischemia due to vascular abnormalities such as pregnancy with eclampsia, severe sepsis, pancreatitis, or other severe shock state [58].

The combination of renal and body ultrasound can help to distinguish different types of AKI, as described in Figure 5. This stepwise approach can help providers methodically investigate AKI from the context of ultrasound and hopefully provide improved patient care.

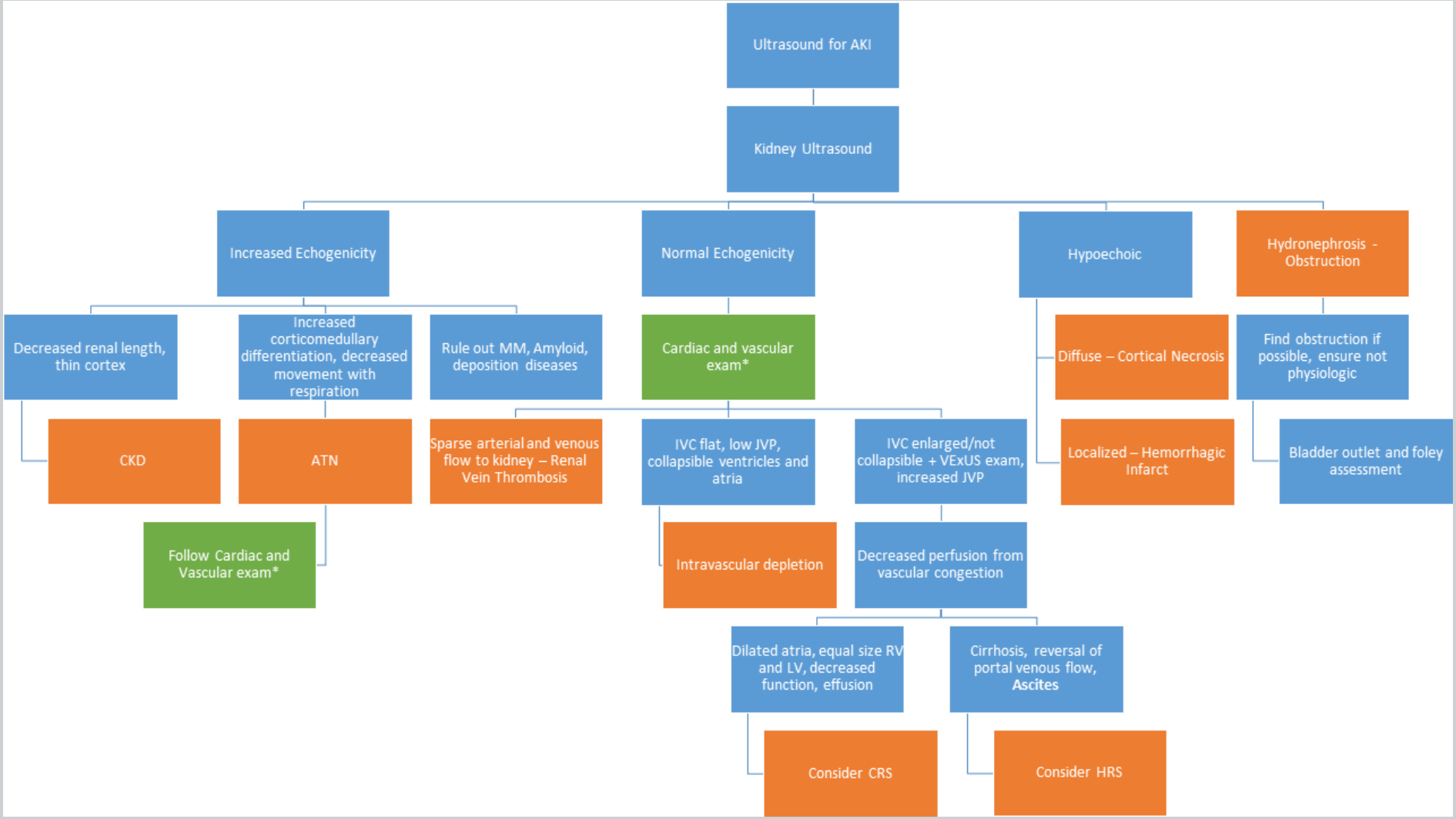
Ultrasound for AKI
Kidney Ultrasound
Increased Echogenicity
Normal Echogenicity
Hypoechoic
Hydronephrosis - Obstruction
Decreased renal length, thin cortex
Increased corticomedullary differentiation, decreased movement with respiration
Rule out MM, Amyloid, deposition diseases
Cardiac and vascular exam*
Diffuse – Cortical Necrosis
Find obstruction if possible, ensure not physiologic
CKD
ATN
Sparse arterial and venous flow to kidney – Renal Vein Thrombosis
IVC flat, low JVP, collapsible ventricles and atria
IVC enlarged/not collapsible + VExUS exam, increased JVP
Localized – Hemorrhagic Infarct
Bladder outlet and foley assessment
Follow Cardiac and Vascular exam*
Intravascular depletion
Decreased perfusion from vascular congestion
Dilated atria, equal size RV and LV, decreased function, effusion
Cirrhosis, reversal of portal venous flow, Ascites
Consider CRS
Consider HRS

Figure 5. Flowsheet on the approach to AKI and ultrasound. Using this flowsheet and starting with a kidney ultrasound, one can decipher most causes of AKI.

Future directions of ultrasound

Ultrasound as a therapeutic

Ultrasound has long been used by physical therapy as a modality to improve local swelling and inflammation. The application of ultrasound alone appears to have postinjury modulation and prevents inflammation in the kidney by stimulating the splenic cholinergic anti-inflammatory pathway [59]. Indeed, it has been shown in mice to markedly attenuate kidney ischemia-reperfusion injury [60]. While these studies were performed in mice and have not been validated in humans, the use in muscle and joints is well established in the physical therapy community and is likely to be applicable in humans.

Contrast-enhanced Ultrasound

Contrast for ultrasound has been used to enhance image intensity from the vasculature. It can give more information on kidney perfusion and microvascular function as well as help localize injury. The newest forms of contrast are gas-filled microbubbles that are surrounded by a shell that is quickly metabolized and the gas exhaled. It is an attractive option as it is non-toxic, does not expose the patient to radiation, and can be done at the bedside. It does require proprietary contrast-specific software which can inhibit its use in resource-limited areas. It has been used to better image lesions in the kidney and to predict acute rejection in transplant patients [61, 62]. Another intriguing possible use is targeted contrast agents with disease-specific antibodies using the signal intensity as correlation with the extent of injury or disease [63]. These disease-specific microbubbles are also being looked at to deliver medications to local sites via locally increased permeabilization [59]. Further translational research is needed, but the outlook is currently promising.

Case example 1

Patient is a 30-year-old male with a past medical history of familial intrahepatic cholestasis and a liver transplant 21 years prior. He has CKD presumed secondary to calcineurin inhibitor use with a baseline creatinine of 1.3-1.5 mg/dL. He also has chronic pancreatitis, developmental delay, and malabsorption with a PEG tube. He presents to your care post-procedure after a failed clipping of a gastric fistula. Following the gastric fistula procedure, the patient was found to have AKI with

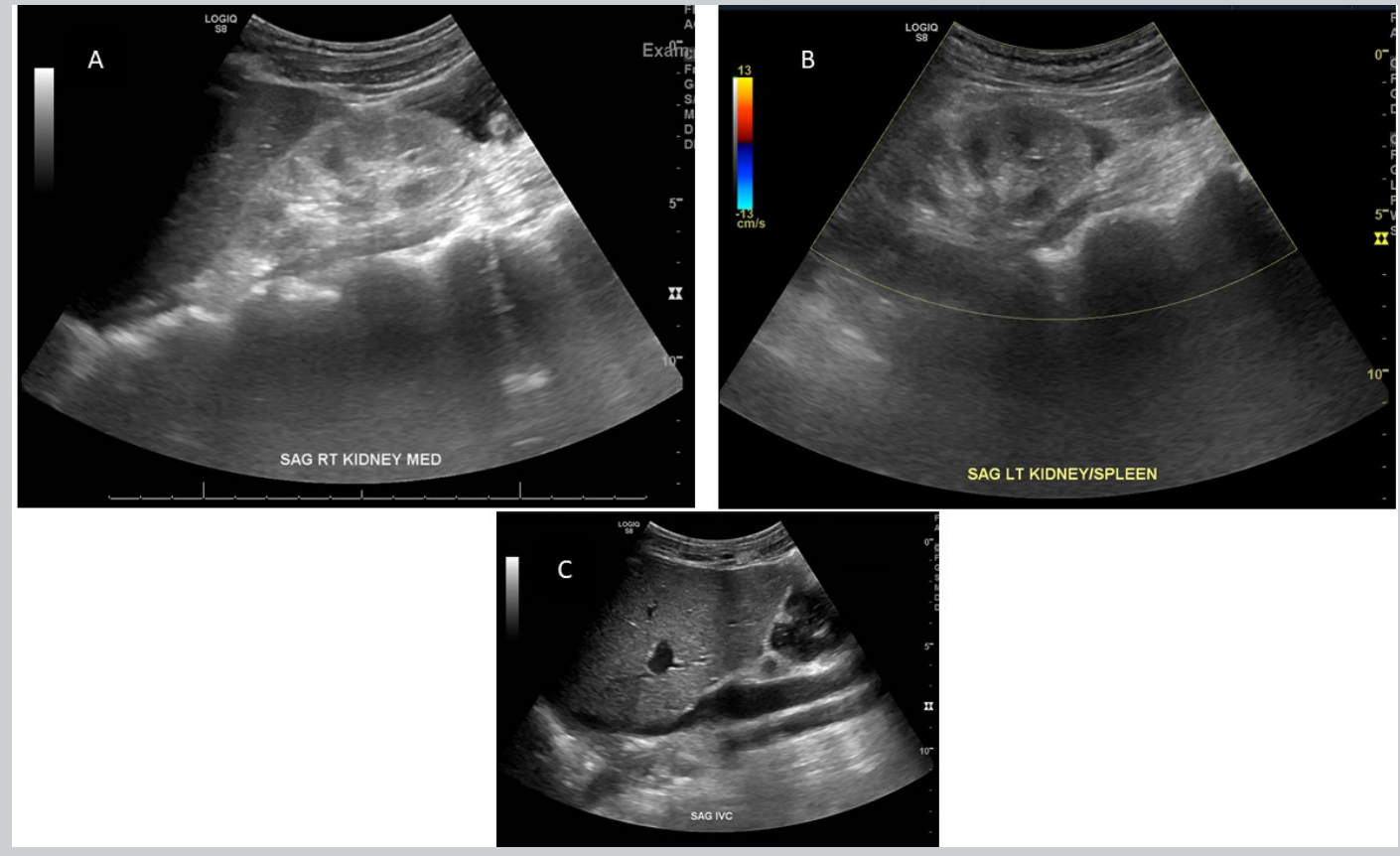

Figure 6. Bilateral Kidney and IVC: Case 1. A) The right kidney appears more echogenic compared with the adjacent liver and has increased medullary pyramid differentiation consistent with ATN. B) Left kidney also with increased echogenicity and differentiation. C) Liver, IVC, and aorta in view. IVC collapsibility index >50%. JVP on ultrasound also found to be at the level of the clavicle (not shown).

creatinine rise from baseline to 6.06 mg/dL. The patient's physical exam is normal except for prior PEG tube site with clean and dry bandage overlying. Vital signs are within normal limits. On review of medication and discussion with patient, no nephrotoxins are identified. Kidney ultrasound is performed (Figure 6) and the radiologist's reading notes bilateral echogenic and atrophic kidneys, likely related to chronic kidney parenchymal disease without hydronephrosis or nephrolithiasis, presumed to be progression of disease. On review by the nephrologist, the kidney cortex is not diminished and there is increased differentiation of the medulla to the cortex, with kidney length likely within in the normal limits of this smaller adult. Given this, a vascular exam was performed which showed multiple signs of intravascular volume depletion, including an IVC with collapsibility index >50%, JVP at the clavicle, and clear lung exam without B-lines. This was consistent with a history of gastrointestinal losses with likely occult hypotension resulting in AKI from pre-renal volume depletion and hypotension. The patient was volume resuscitated, but continued to have a rise in creatinine to a peak of 12.49 mg/dL. Lack of response to volume challenge indicated that the patient had been volume deplete for some time, ATN had likely occurred from prolonged kidney ischemia. However, his kidney function recovered back to baseline once ongoing gastrointestinal losses stopped and intravascular fluid was successfully repleted.

Ultrasound is currently underutilized in AKI. It is not only able to diagnose obstruction, but it can also yield important data on underlying CKD status, vascular status, ATN, and inflammatory states of the kidney. The most important aspect of ultrasound is its ability to be performed quickly at the bedside throughout the hospital stay, helping to monitor response to therapeutics and aid in diagnosis as changes occur. The ultrasound itself may eventually be used as a therapeutic and contrast-enhanced ultrasound can both enhance diagnosis and may be used to deliver therapeutics as well. It has become an invaluable tool in the clinician's tool kit.

Disclosures

None

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Review

Focused Cardiac Assessment in Kidney Care

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Background

Point of care ultrasonography (POCUS) is considered to be a very useful and informative extension of the bedside physical exam. The information obtained from POCUS allows for real time assessment for expedited decision making to improve efficiency in patient care and management. Many programs across the country are now incorporating POCUS into their training schedules to allow their residents, fellows, and faculty to gain competence in the techniques and varied clinical uses of POCUS [1-3]. In nephrology, POCUS has been used at the bedside for access planning, dialysis catheter placement, and to guide kidney biopsies to mention a few applications [4]. There is a wide scope for POCUS in nephrology in addition to kidney and bladder assessment. This includes focused cardiac ultrasound to evaluate the heart for structural and functional abnormalities and lung ultrasound as well. These bedside ultrasound assessments help with point of care management decisions pertaining to volume assessment in acute and chronic kidney disease, adjustment of ultrafiltration goals in dialysis patients, and evaluation of hypotension and dyspnea.

This review describes the techniques, interpretation, and application of focused cardiac ultrasound for the nephrologist (FoCUS).

Ultrasound Probe

A fundamental component of ultrasound imaging is choosing the right transducer or probe. The probe used for cardiac assessment is made from piezoelectric crystals which generate fine vibrations in a phenomenon called reverse piezoelectric effect [5]. These vibrations are converted to ultrasonic waves that are transmitted to the tissue and then reflected back to the probe. This effect causes mechanical distortion of the crystals, which is converted to an electric current and then used by the ultrasound machine to generate an image [6].

Transducer types: Ultrasound transducers differ in construction based on piezoelectric crystal arrangement, aperture (footprint), and frequency. The transducer used for cardiac ultrasound is a phased array transducer which produces diverging low frequency ultrasound beams (1 to 5 MHz) that generate a pie shaped format with room for focus adjustment and steering. Differential excitation of the piezoelectric crystals creates rapid electronic beams by sequentially pulsing multiple small crystals within the transducer. This technology allows for efficient two dimensional imaging and is optimal for structures such as the heart.

Views in Cardiac Imaging

Cardiac ultrasound requires assessment of both structure and function of the heart and the highest quality images should be acquired for optimal assessment. In order to be confident in the interpretation of cardiac ultrasound findings, views from multiple imaging planes should be obtained. Traditional teaching focuses on achieving proficiency in five core cardiac views: parasternal long axis (PLAX), parasternal short axis (mid ventricular level) (PSAX), apical 4-chamber (A4C), subcostal 4-chamber (S4C), and subcostal inferior vena cava (IVC) views [7]. Images from these views are shown in Figure 1.

Imaging Windows and Views

PARASTERNAL WINDOW

Traditionally cardiac ultrasound begins with the parasternal window. Ideally, the patient should be placed in a supine position, but if needed the patient can be made to lie in the left lateral decubitus position to bring the heart in direct contact with the chest wall.

Parasternal long axis view (PLAX): This is obtained by placing the phased-array probe immediately to the left of the sternum in the third or fourth intercostal space (ICS) with the probe marker pointing towards the right shoulder. The beam should be positioned parallel to a line running from the patient's shoulder to the left hip. The appropriate window for imaging may lie anywhere between the second to the fifth intercostal spaces and sliding might help get the best images possible where the mitral valve should be positioned in the center of the ultrasound image. An ideal parasternal window has appropriate positioning of the cardiac structures and the least interference from the adjacent organs including the lung. Images obtained from this view demonstrate the anatomic cross-section of the long axis of the heart and include the aortic valve (AV), mitral valve (MV), left ventricle (LV), pericardium, right ventricular outflow tract (RVOT), left ventricular outflow tract (LVOT), and portions of the ascending and descending aorta (AO).

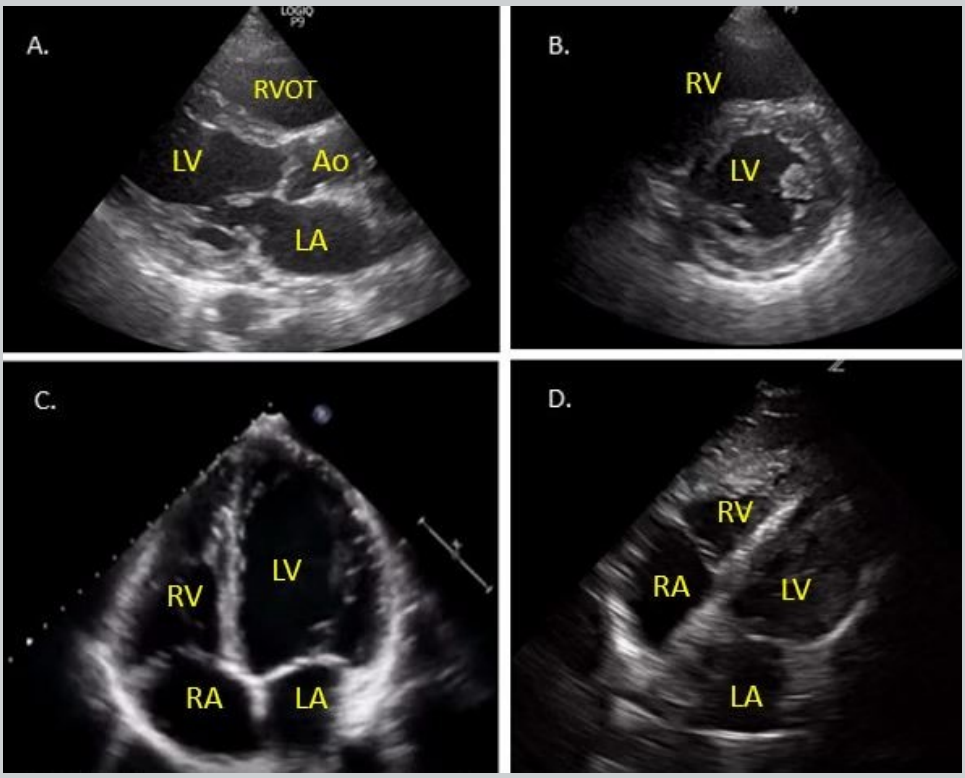

Figure 1.
A) Parasternal long axis view.
B) Parasternal short axis view.
C) Apical 4-chamber view.
D) Subcostal 4-chamber view.
LA - left atrium, LV - left ventricle, RA - right atrium, RV - right ventricle, RVOT - right ventricular outflow tract, Ao - aorta.

The right ventricle (RV) is visualized at the top of the screen. While keeping the probe steady, the mitral and the aortic valves can be seen and the ultrasound beam can be centered on the left ventricle. With slight rotation and tilting movements of the probe, the left ventricular cavity can be analyzed in its full extent. PLAX view is used primarily to assess LV size and function in addition to the AV, MV, and left atrial size. Circumferential pericardial effusions can also be detected in this view. However, assessment of right ventricle size and function is difficult from this view.

Parasternal short axis views (PSAX): An effective technique to acquire high-quality PSAX views is by starting with high-quality PLAX views. The probe is then rotated 90 degrees clockwise to point towards the patient left shoulder. Care must be taken not to allow the transducer to slide to a different position on the chest. The 2-hand maneuver can be tried so as to keep the transducer steady with one hand while the other hand rotates the transducer into position. While five different imaging planes can be achieved in the parasternal short axis view, the mid ventricular level is favored by most providers for its reliable portrayal of LV function. Mid-ventricular parasternal short axis view is achieved when both papillary muscles are visualized in cross-section and appear symmetric. The short axis mid-ventricular view is best for assessing global LV systolic function and segmental LV wall motion. This view also helps assess the shape and function of the interventricular septum in the setting of RV dilatation and dysfunction. Large or moderate sized circumferential pericardial effusions can also be visualized.

Pulmonary artery level: From the mid-ventricular level the ultrasound beam is tilted towards the base of the heart. The plane is considered correct when the pulmonary valve (PV), main pulmonary artery (MPA), and AO are seen in short axis. In this view, pulmonary regurgitation velocities may be used to estimate the mean and diastolic pulmonary artery pressures.

AV level: From the pulmonary artery level, the transducer is tilted slightly inferiorly towards the apex of the heart. An ideal image includes short axis view of the AV, which may require a slight rotation of the transducer until all 3 AV cusps appear symmetric. This view allows assessment of AV and TV (Figure 2).

MV level: When rotating from parasternal long axis to short axis view, the distinct fish mouth appearance of the MV is usually seen first which allows for an assessment of the MV (Figure 2).

Mid-ventricular, papillary muscle level: This view reveals the most useful clinical information in vast majority of acutely ill patients. Papillary muscles are symmetrically seen in cross-section in the center of the circular left-ventricular cavity. Motion of individual LV chamber wall segments is best assessed at this level, as well as overall LV systolic function (Figure 2).

Apical level: The short axis view is obtained by tilting the transducer to aim the ultrasound beam inferiorly, towards the apex of the heart. The left ventricular apex is visualized sequentially starting from the mid papillary muscle level and moving inferiorly. LV systolic function

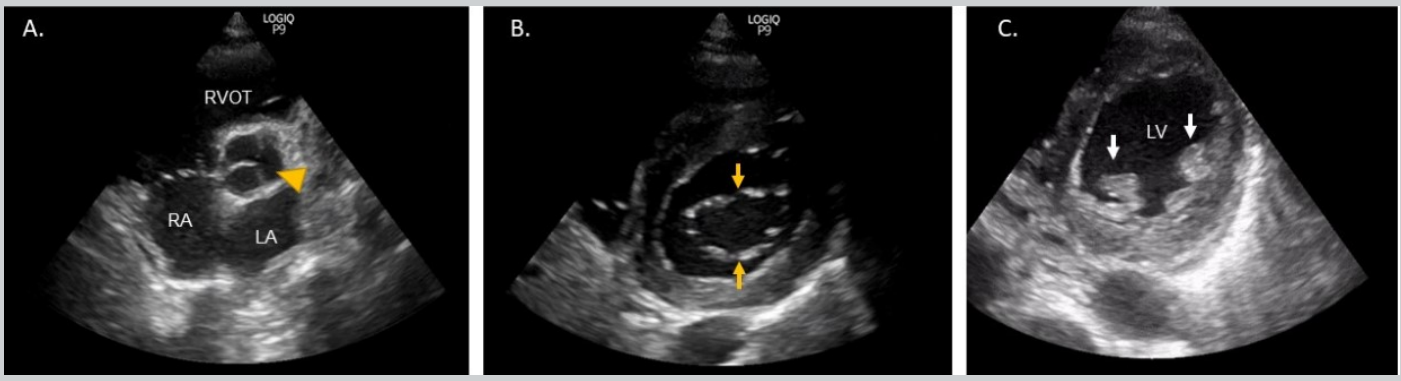

Figure 2. Parasternal short axis (PSAX) view at the level of A) aortic valve [arrowhead], B) mitral valve [arrows point to the valve leaflets], and C) papillary muscle/mid-ventricle [arrows point to papillary muscles]. RA: right atrium, LA: left atrium, RVOT: right ventricular outflow tract, LV: left ventricle.

may be overestimated compared to the mid ventricular level. In rare cases an apical LV thrombus may be seen.

APICAL WINDOW

Imaging window: The apical window usually follows the parasternal views. It is more difficult to obtain quality images from an apical window when compared to parasternal or subcostal windows.

Apical 4-Chamber View

With the patient either in the left lateral decubitus position or supine with subtle leftward rotation, the probe is placed over the cardiac apex (inferolateral to the left nipple in males and below the inferolateral quadrant of the left breast in females). Once the apex is visualized, the transducer needs to be tilted steeply to aim the orientation marker to the patient's left side.

Once positioned in the apical area, the transducer should be rocked to align the interventricular septum in a vertical position in the center of the screen. The transducer might need to be rotated slightly so that the LV and RV cavities are viewed in a true longitudinal cross-section. In an ideal apical 4-chamber view the LV, RV, LA, and RA can all be seen clearly in addition to the MV and TV. The apical 4-chamber view helps in assessment of the RV and its systolic function. MV and TV can also be evaluated and pericardial fluid can be detected.

Apical 2-Chamber View

Starting from an apical 4-chamber view, the transducer is rotated 90 degrees counterclockwise. The ideal view reveals LV, LA, and MV. Under rotation or over rotation can reveal RV or LVOT respectively. This view allows assessment of the regional LV function.

Apical 3-Chamber View

Starting from an apical-2 chamber view, the transducer is further rotated 30 degrees counterclockwise. The ideal view demonstrates the LV, LA, and MV with the LVOT and AV appearing at the 5 o'clock position. Assessment of the inferolateral and anteroseptal LV walls can be ascertained from this position.

SUBCOSTAL WINDOW

In the subcostal view, the transducer is placed below the xiphoid process in the midline with the probe marker pointed to the patient left side. The ultrasound transducer face should be aimed upward towards the heart and left shoulder. Asking the patient to bend their knees to relax the abdomen or holding their breath momentarily at end of inspiration can transiently shift the heart downward into view.

Subcostal 4-Chamber View

Once the heart is in view in the subcoastal window, subtle transducer manipulation can help in acquisition of an optimal 4-chamber view. Ideally the RV, LV, RA, LA, and pericardium should be visualized in cross section along the long axis of the heart. This view can help assess the RV free wall and perform a comparison of LV and RV size. However, as the imaging plane is through the inferior portion of the heart rather than the middle of the heart, RV size can be underestimated. This view also allows for visualization of pericardial effusion.

Inferior Vena Cava View

Once the traditional subcostal view is obtained, the transducer is rotated 90 degrees counterclockwise, so the orientation marker is directed cephalad. With subtle adjustments and while not losing view of the right atrium, the IVC comes into focus with the RA-IVC junction on the screen. An ideal subcostal view also demonstrates the hepatic veins emptying into the IVC, along with the IVC emptying into the RA.

Measurements

Left Ventricular Systolic Function Assessment

Assessment of left ventricular systolic function includes calculation of the stroke volume and also ejection fraction. The steps involved in this assessment are as follows:

Measurement of Left Ventricular Outflow Tract (LVOT)

Measurement of left ventricular outflow tract diameter is crucial for assessment of left ventricular systolic function. Once PLAX views are obtained, focus is directed towards the aortic valve and the LVOT to capture the maximal opening of the AV valve in mid-systole. The diameter of the LVOT at the base of the AV is measured. The LVOT area is calculated based on the equation below [8].

LVOT area = π x (radius of LVOT)^2

Measurement of Velocity Time Integral (VTI)

Once apical 4-chamber views are obtained, with slight manipulation of technique, apical 5 chamber views can be obtained. Once this view is obtained, pulse wave doppler can be centered in the LVOT to obtain the LVOT systolic flow velocity. Once the systolic flow velocity is traced, the machine software can calculate the area under the curve which will results in estimation of the velocity time integral (VTI). The VTI (measured in centimeters) represents the distance blood is propelled forward from the LVOT to the aorta with each cardiac contraction.

Calculation of Stroke Volume

Once the LVOT diameter and VTI have been entered into the ultrasound, the available software calculates the left ventricular stroke volume (LVSV) according to the equation:

LVSV (cm^3) = LVOT Area (cm^2) X LVOT VTI (cm)

The formula is derived from the volume of a cylinder while considering that LVOT is the area of the cylinder and VTI represents the height of the cylinder, so the LVSV is a product of these two measurements.

EPSS (E-Point Septal Separation)

The major chambers on the left side of the heart, the left atrium and left ventricle, are separated from each other by the mitral valve. The mitral valve is made up of two leaflets: anterormedial and posterolateral. The mitral valve is typically 4-6 cm^2 in area. In the PLAX view, using the M-mode (motion mode), the cursor is placed through the mitral valve. In order of sequence (from top to the bottom) the RV, interventricular septum, anterior mitral valve leaflet, and posterior ventricular wall can be seen. The first peak (E-wave) noted during mitral valve tracing is the passive diastolic filling of the left ventricle while the

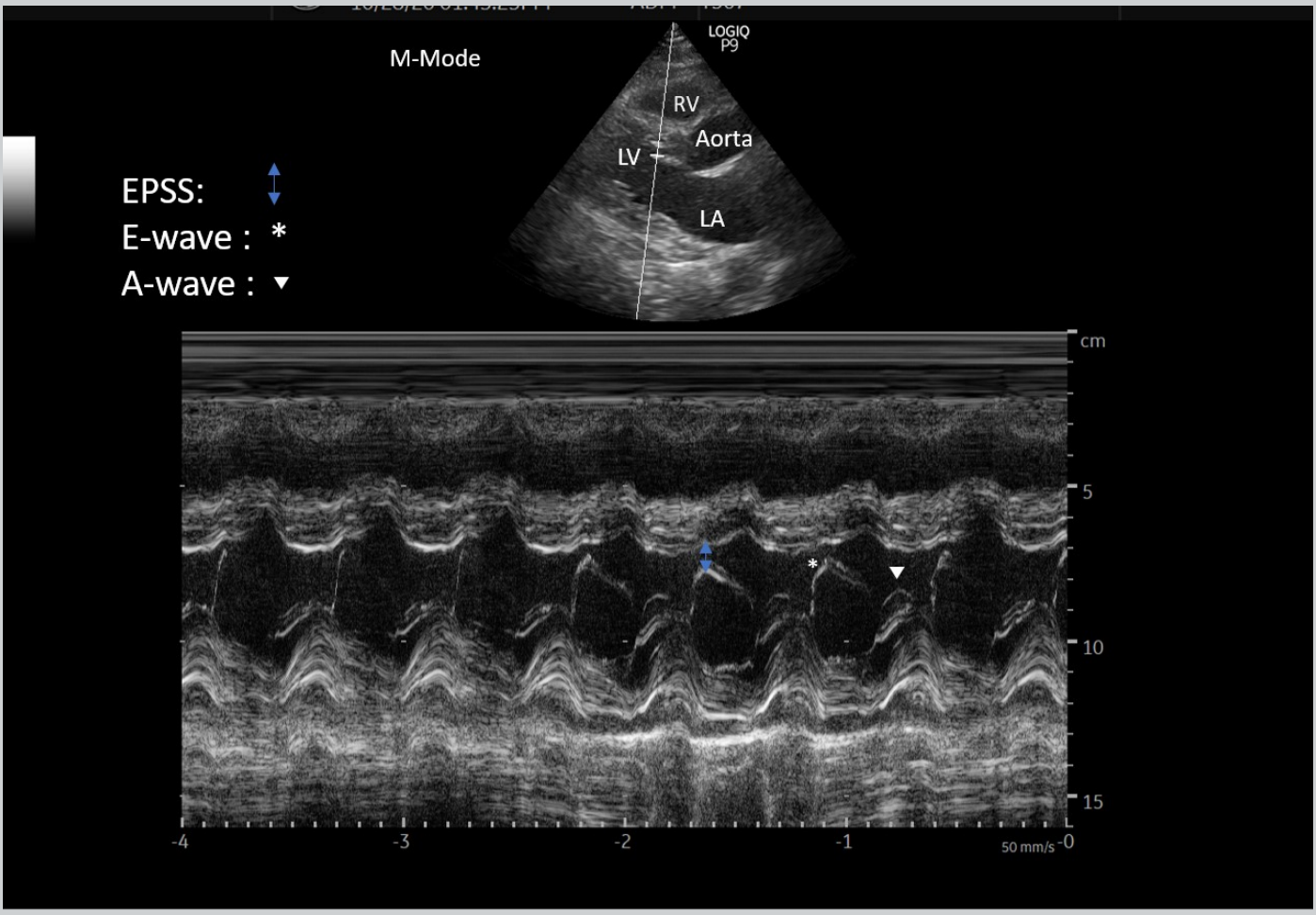

Figure 3. E point septal separation-definition and measurement.

following, smaller A-wave represents LV filling from LA contraction. EPSS represents the distance separating the peak height of the E-wave from the interventricular septum during early diastolic filling. EPSS can be thought of most simply as inversely correlated with left ventricle contractility and ejection fraction. A normal, healthy anterior MV leaflet may come in contact with the septum creating zero distance of E-point separation. An EPSS greater than 7 mm may be used to predict patients with severely reduced LVEF [9]. The technique for measurement of EPSS is shown in Figure 3.

Tricuspid Annular Plane Systolic Excursion (TAPSE)

A commonly used parameter for measurement of right ventricular function is called tricuspid annular plane systolic excursion (TAPSE). In an apical 4-chamber view, the maximum systolic excursion of the lateral tricuspid annulus is measured by M-mode. The tracing can be acquired easily. Though TAPSE varies from individual to individual based on gender and body surface area, a TAPSE < 17 mm is highly suggestive of RV dysfunction [10].

Inferior Vena Cava Measurements (IVC Measurements)

A routine part of POCUS should include IVC measurements. Images are obtained as described above in the subcostal view of the heart. One important aspect to remember while acquiring images of the IVC is to obtain images longitudinally with the transducer centered on the long axis of the IVC to accurately estimate IVC diameter and collapsibility. Imaging outside the longitudinal axis of the IVC will result in oblique view of the vessel and underestimation of the vessel diameter in the so-called "cylinder effect". Using M-Mode, the diameter of the IVC can be calculated. The IVC is subject to great degree of variation due to the effect of the RA. IVC diameter <2.1 cm that collapses >50% suggests normal RA pressure of 3 mm Hg (range, 0–5 mm Hg), whereas IVC diameter >2.1 cm that collapses <50% with a sniff suggests high RA pressure of 15 mm Hg (range, 10–20 mm Hg) [11]. IVC measurement may not reliably predict right atrial pressure and volume status in patients who have intraabdominal hypertension, acute excerbation of airways disease such as asthma or COPD, right ventricular failure, or pericardial tamponade as well as those on positive pressure ventilation. Similarly, in conditions of severe tricuspid regurgitation and pericardial constriction, there is likely to be a discordance between IVC measurements and the actual volume status of a patient. Incorrect techniques of image acquisition, movement of the transducer while using M-mode and lateral sliding of the IVC relative to the transducer with inspiration may introduce additional sources of error that operators and interpreters must keep in mind [18].

Clinical Application of FOCUS in Nephrology Practice

Emergency medicine programs use the 5E's mnemonic to gather valuable information from FOCUS which includes effusion, ejection, equality, exit, and entrance. Applying this information to clinical nephrology can help

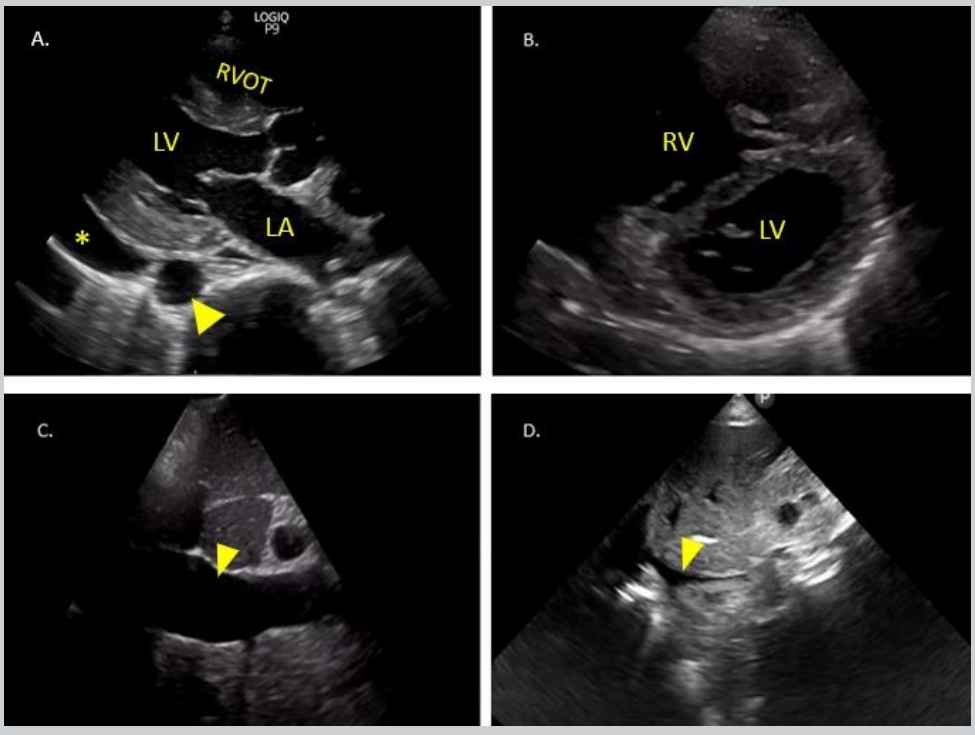

Figure 4.

A) Pericardial effusion (*) in the PLAX view. Arrowhead denotes descending thoracic aorta.

B) D-shaped LV in RV overload (interventricular septal flattening).

C) Plethoric IVC (arrowhead).

D) Collapsible IVC (arrowhead).

LA - left atrium, LV - left ventricle, RV - right ventricle, RVOT - right ventricular outflow tract, IVC - inferior vena cava.

in a variety of scenarios described below that are frequently encountered on the nephrology consult service and dialysis rounds. A few representative images of abnormalities that may be seen on FoCUS are depicted in Figure 4.

Dyspnea: Dyspnea is a common presenting complaint in patients with kidney disease [12]. The differential for dyspnea is broad and includes, amongst other causes, LV dysfunction (leading to pulmonary edema), acute RV strain (in the setting of pulmonary embolism), valvular disorders (for example, mitral regurgitation), or pericardial effusion. Prompt bedside FoCUS can help delineate these different etiologies of dyspnea and guide further management as clinically indicated.

Hypotension: Hypotension is frequently encountered in dialysis patients [2, 13] and this is also a risk factor for development of hemodynamic acute kidney injury [14]. Hypotension can also manifest in the different types of shock seen in critically sick patients which may be challenging to differentiate clinically. FoCUS can help rapidly identify the etiology of shock as cardiac versus non-cardiac and guide initiation of appropriate protocols for treatment in a timely and efficient manner.

Volume management: The need for volume assessment and assistance with management is a frequent reason for requesting nephrology consultation in the hospital. IVC assessment has been shown to correlate well with RAP [11]. The caveat here is that IVC assessment needs to be interpreted in the appropriate clinical context and may not provide accurate estimation of the volume status in some scenarios including mechanically ventilated patients [11] and those with intraabdominal hypertension [15]. Serial measurements of the IVC can help in guiding diuretic management in fluid overloaded patients. Also, IVC assessment in dialysis patients can help add precision to adjustment to ultrafiltration goals and estimated dry weight with dialysis [16].

In conclusion, FoCUS is an attractive modality for the busy nephrologist with the ability to provide quick, point of care answers to common clinical questions.

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Review

POCUS in Intensive Care Nephrology

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Abstract

Acute kidney injury (AKI) is a significant problem for patients admitted to the intensive care unit (ICU), both due to the high incidence and associated mortality with rates of AKI requiring renal replacement therapy (RRT) of over 5%, and mortality rates with AKI of over 60% [1,2]. Ultrasound can be used to identify those at risk for AKI and assist with AKI management. Risk factors for AKI in the ICU not only include hypoperfusion but also venous congestion and volume overload. Volume overload and vascular congestion are associated with multi-organ dysfunction and worse renal outcomes. Daily and overall fluid balance, daily weights, and physical examination for edema can be inaccurate and belie true systemic venous pressure [3-5]. Bedside ultrasound allows providers to evaluate vascular flow patterns and obtain a more reliable evaluation of volume status to guide and individualize therapies. Cardiac, lung, and vascular patterns on ultrasound can identify preload responsiveness, which should be assessed to safely manage ongoing fluid resuscitation and assess for signs of fluid intolerance. Here we present an overview in the use of point of care ultrasound with particular emphasis on nephro-centric strategies, namely in the identification of the type of renal injury, renal vascular flow assessment, the static measure of volume status, as well as dynamic evaluation for volume optimization in critically ill patients.

1. Diagnosis and management of acute kidney injury using point of care ultrasound (POCUS)

Acute kidney injury is a pervasive issue for patients admitted to the intensive care unit (ICU). Not only is it common, but it is also associated with high mortality rates of up to 60%, so early recognition and optimization of renal resuscitation is paramount [1,2]. Bedside ultrasound assists with determining the etiology for AKI and allows providers to evaluate vascular flow patterns to obtain a reliable evaluation of volume status and guide individualized therapies to help improve renal outcomes.

Hemodynamic AKI

Hemodynamic AKI involves hypoperfusion and is attributable to hypovolemia or low oncotic states seen in heart or liver failure. Cardiac ultrasound can be highly beneficial to help further delineate between these potential etiologies. The ejection fraction depends on ventriculo-arterial coupling, thus is determined by both intrinsic cardiac function and the afterload state [6]. As such, hyperdynamism, or an ejection fraction >70%, may be seen either in states of hypovolemia or vasoplegia as seen in liver failure or sepsis. Heart failure on the other hand is not typically associated with a hyperdynamic heart [7]. If hyperdynamism is visualized, performing a left ventricular outflow tract (LVOT) velocity time integral (VTI) measurement can help distinguish between hypovolemia and vasoplegia. A low VTI, or one <18 cm, is consistent with low stroke volume and low cardiac output, as seen in hypovolemia. Conversely, a high VTI, or >22cm, is more consistent with a high output state as seen with vasoplegia and distributive shock (Figure 1) [8].

Intrinsic AKI

Renal Resistive Index

The renal resistive index (RRI) evaluates the resistance to flow and as such can be used to assess macrovascular perfusion to the kidney. The RRI is obtained at the level

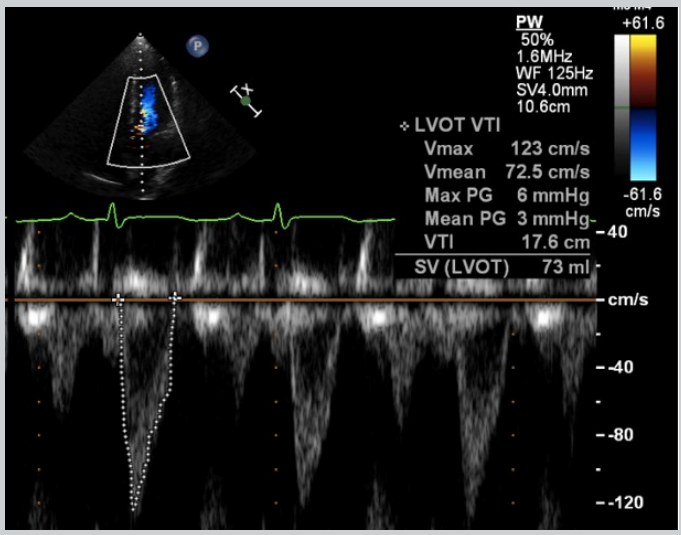

Figure 1. LVOT VTI calculated by obtaining a 5-chamber apical view and using a pulsed-wave Doppler at the opening of aortic valve to trace along the edge of the velocity to measure the area under the curve.

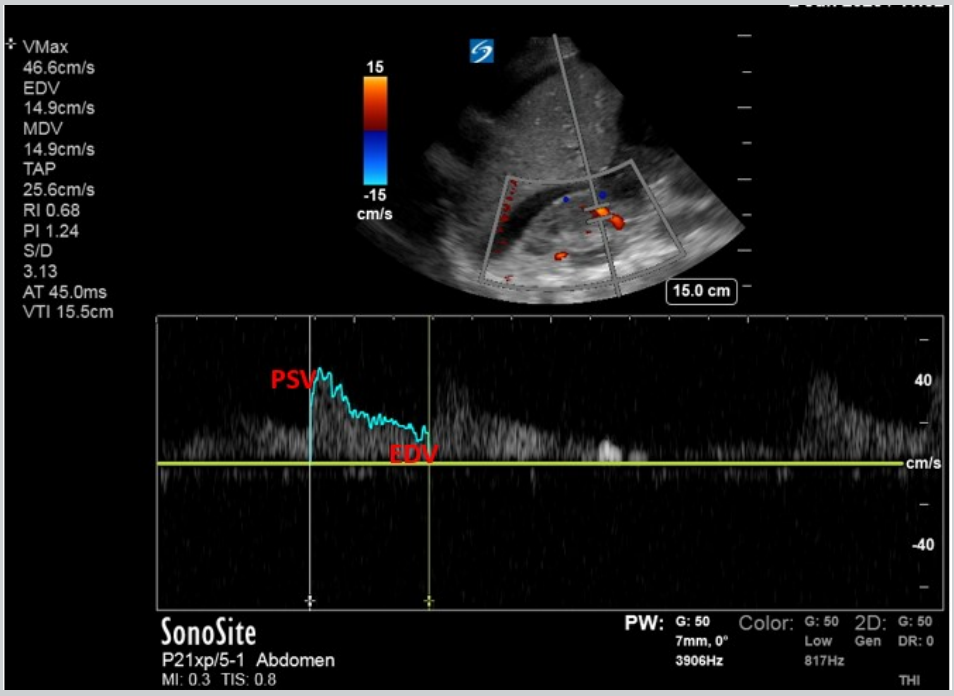

Figure 2. Renal Resistive Index (RRI) can be calculated automatically by ultrasound or plugging into formula: RRI = [(PSV– EDV)/PSV], where PSV = peak systolic velocity, EDV = end diastolic velocity.

of the segmental arteries and is calculated as follows [9]:

RRI = [(peak systolic velocity – end diastolic velocity)/ peak systolic velocity]

Normal values are roughly 0.6 with levels >0.70 used as a cut-off for an abnormal value in native kidneys and 0.8 in transplanted kidneys (Figure 2). Higher levels portend to worse renal outcomes and are predictive for AKI in general as well as for severity of AKI in various patient populations [9-12].

The RRI may be increased in CKD or AKI when due to obstruction, acute rejection, hepatorenal syndrome, or acute tubular necrosis (ATN) [9]. The RRI can be helpful to distinguish between AKI secondary to pre-renal azotemia, where it remains normal, compared to ATN when it is often elevated [13]. Studies have shown a resistive index >0.75 correlates to a diagnosis of ATN with over 90% of patients having ATN compared to only 20% with pre-renal azotemia, most of which had hepatorenal syndrome [9,12-16].

The RRI has several limitations. Firstly, it can be affected by heart rate as tachycardia can falsely elevate the end diastolic pressure and thus falsely decrease the RRI [17]. The RRI may also be affected by increased intraabdominal pressure, medications, and the location where it is measured [18,19]. Previous studies have shown reproducibility of RRI among different operators, however most studies involved expert sonographers and intra-observer variability may exist in novice sonographers [20,21]. Lastly, while the RRI evaluates macrovascular perfusion, it is unable to assess slow flow velocities in vessels <2 mm and microcirculatory perfusion plays an important role in AKI due to sepsis [22,23].

Post-renal AKI

Hydronephrosis

Ultrasound is the main imaging modality to evaluate for hydronephrosis, which causes 1-3% of AKI in the ICU and is seen on ultrasound in up to 95% of patients with obstruction [25-28]. There are different degrees of hydronephrosis including mild, moderate, and severe with varying degrees of disruption of the pelvicalyceal system (Figure 3) [10,29]. Of note, it is critical to place color Doppler over the kidney as renal vasculature or vascular malformations can easily mimic hydronephrosis (Figure 3). Although AKI in the setting of obstructive uropathy in the ICU is rare, it is a potentially reversible cause of AKI that can change your management. Ultrasound is a vital tool to make this diagnosis quickly at the bedside that should be employed by every provider for any patient presenting with AKI.

2. Nephroprotective strategies

While it is important to correct hypovolemia and supplement preload during early management, particularly for distributive and hypovolemic shock, guiding ongoing fluid administration after the initial resuscitation can be nebulous and nuanced. It has been proposed by Malbrain et al. that there are several stages of fluid management, or the 4 D's. These include drug, dosing, and duration which revolve around the type and amount of fluid resuscitation as well as de-escalation as it relates to fluid removal [29]. POCUS can be used during both the resuscitative and de-resuscitative stages

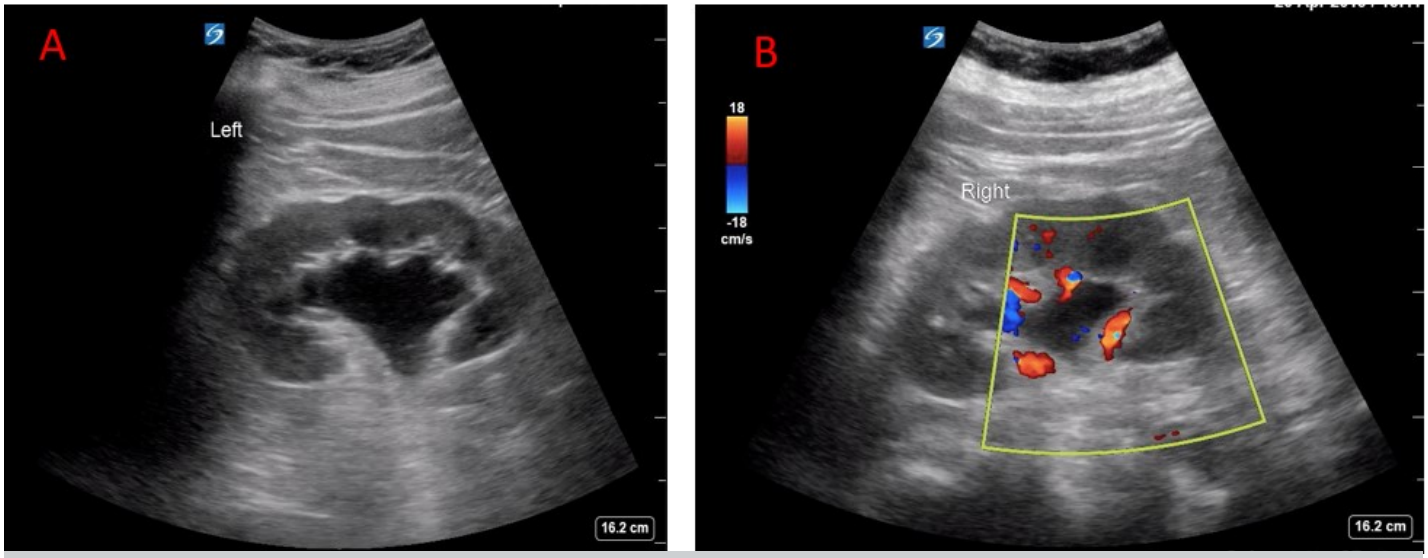

Figure 3. A) Example of moderate hydronephrosis, B) Example of hydronephrosis with color to rule out vasculature.

of management.

The use of POCUS to optimize resuscitation

Static markers such as CVP were used in the past, however, have not been shown to reliably identify patients that benefit from the administration of fluids [30]. As such, there is an emphasis on using dynamic measures to assess for fluid responsiveness, which is defined as an increase in cardiac output or cardiac index by 15% or more in response to a fluid challenge. Many of these dynamic measures used to evaluate for fluid responsiveness rely on heart-lung interactions during mechanical ventilation and involve the use of ultrasound. It is important to note limitations for the following assessments of fluid responsiveness as they can be affected by spontaneous breathing, arrhythmias, or low tidal volume ventilation [31-36].

Venous System – Inferior Vena Cava

The inferior vena cava (IVC) should be viewed in long axis from the subcostal position with measurements taken 2 cm distal to the junction with the right atrium, or just distal to the inlet of the hepatic vein. Due to differences in IVC collapsibility by sampling location and displacement associated with respirophasic cycles multiple measurements at different levels should be taken, including the short axis (Figure 4) [37,38]. There have been many studies looking at the IVC for fluid responsiveness and the best evidence exists for patients on mechanical ventilation [39,40]. IVC collapsibility, when used in spontaneously breathing patients, loosely correlates to CVP and acts as a static measure of volume status. Conversely, given the vessel distends on receiving a mechanical breath instead of collapsing, IVC distensibility assesses vessel compliance in addition to right atrial pressure and the transmural gradient between intraabdominal and intrathoracic pressures. The IVC distensibility thus provides a better assessment for volume responsiveness from a physiologic perspective for patients on mechanical ventilation compared to those with spontaneous respirations, and multiple studies

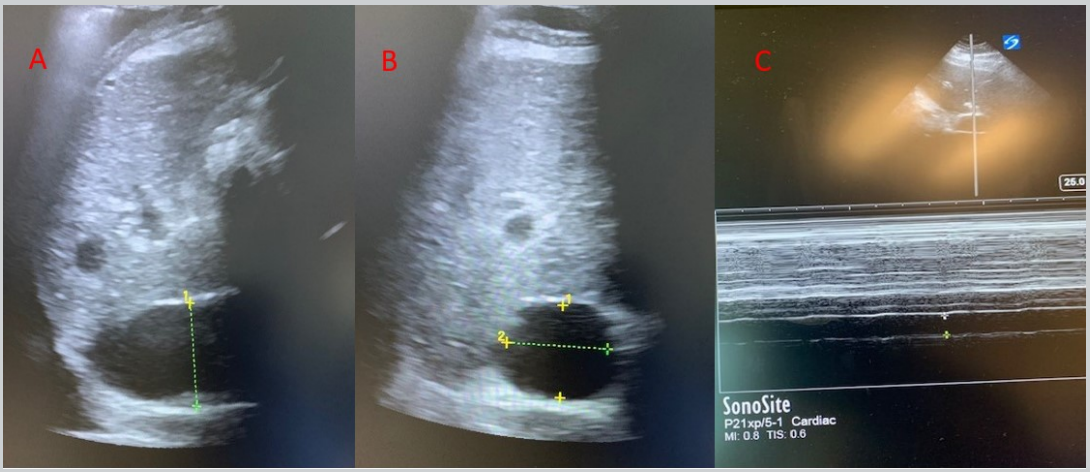

Figure 4. A) IVC-long axis view, B) IVC-short axis view, C) IVC- M-mode to assess for respiratory variation and collapsibility.

support this physiologic rationale [41].

Measurement of IVC size and its collapsibility can act as a surrogate measure for CVP and RAP where a size >2.1 cm with <50% collapsibility indicates a CVP of 15. Conversely, an IVC <2.1 cm with >50% collapsibility is consistent with a normal RAP of 3 mmHg [41]. An underfilled IVC can help identify hypovolemia, particularly in patients with known volume losses. In states such as sepsis or liver failure, however, where vasoplegia occurs and there is loss of vascular tone, care should be taken to use measures other than the IVC to determine whether to give additional IVF. In such patients, there is a higher ratio of unstressed to stressed volume, and volume overload would need to occur to manifest any change in the stressed volume as visualized by IVC measurement. Conversely, a plethoric IVC indicates the presence of hypervolemia and can help rule out hypovolemic shock. However, the IVC may be plethoric without the presence of hypervolemia and volume overload when tricuspid regurgitation, elevated right sided heart pressures from elevated pulmonary pressures, and cardiac tamponade are present.

IVC size and collapsibility in spontaneously breathing patients can be affected by elevated intra-abdominal pressures and heavy spontaneous breathing efforts and it is only loosely related to CVP. Careful consideration should be taken when using ultrasound of the IVC in isolation to determine volume status. Rather, it should be used in conjunction with the overall clinical context and constellation of ultrasound findings.

The use of POCUS to optimize de-resuscitation

It is critical to avoid volume overload which causes tissue edema and prolonged ventilator weaning, and is an independent predictor of mortality in ICU patients, particularly those with sepsis, ARDS, intra-abdominal hypertension, and acute kidney injury. As such, de-resuscitation is a critical phase of a patient's ICU management [42-46]. POCUS can be used to guide this phase of therapy.

Cardiac Ultrasound

In addition to assessing the left ventricle (LV), right ventricular size and function should be evaluated, particularly with regards to assessing volume status. Enlargement of the right ventricle (RV) can be either a sign of volume or pressure overload. The parasternal short axis view can be utilized to evaluate which of these processes predominates as septal bowing seen in systole corresponds to pressure overload on the RV, suggesting an etiology such as pulmonary embolism, whereas septal bowing in diastole corresponds to volume overload that should prompt diuresis [47,48].

Diastolic function can also be used to assess volume status where e' maximal velocity reflects the rate of LV relaxation and E/e' correlates to LV filling pressures. There are studies in the ICU showing an abbreviated assessment can be valuable and diagnostic for increased left ventricular end-diastolic pressure (LVEDP) [49,50].

Using pulse-wave Doppler with the gate just above the mitral valve leaflet tips, obtain a spectral waveform. An E < A wave indicates grade 1 diastolic dysfunction (DD) with normal left atrial pressure and thus normal LVEDP (Figure 5). If E > A, perform an e' measurement placing TDI over the septal and/or lateral mitral annulus (Figure 5). An E/e' >15 is consistent with an elevated LVEDP that should prompt diuresis [51,52]. Studies have shown an E/e' >15 in the point of care setting to be 100% sensitive and 95% specific for heart failure when found in conjunction with B lines on lung ultrasound, also

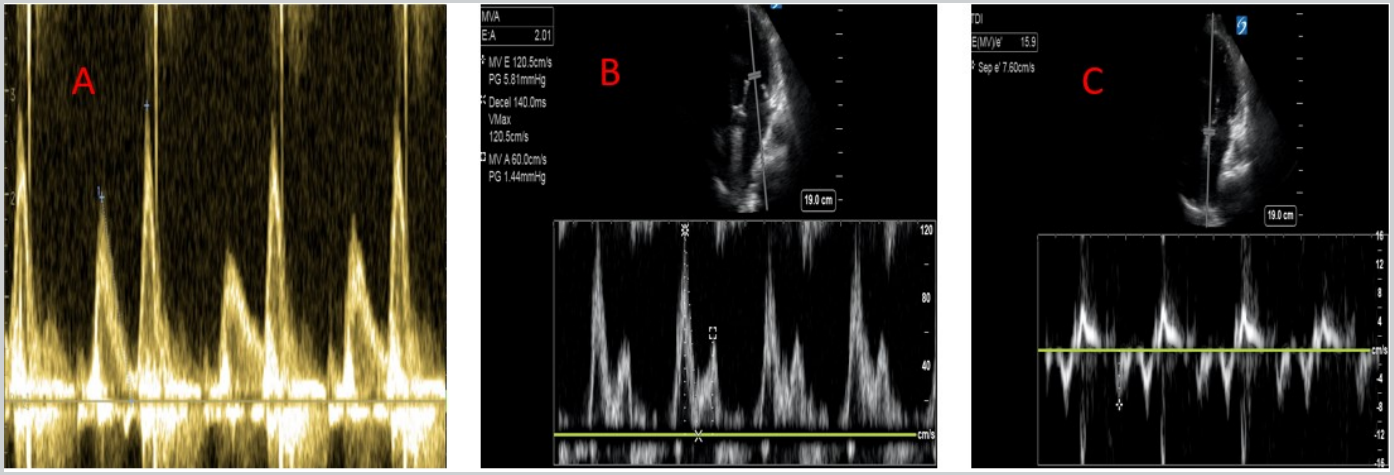

Figure 5. A) Grade 1 diastolic dysfunction showing E<A wave, B) Grade 3 diastolic dysfunction showing E/A wave >2, C) E/e' > 15 consistent with raised LVEDP.

performing better than other modalities such as BNP and chest x-ray for diagnosing decompensated heart failure [51]. Conversely, if the E/e' is <8, then the LVEDP is likely normal [52].

Lung Ultrasound

Depending on one's comfort level with more advanced echocardiography techniques, a lung ultrasound is simple to perform and can also be beneficial in assessing volume status in conjunction with other modalities. The presence of A-lines indicates normal lung aeration with dry interlobular septa and low or normal LAP [53]. A B-profile, on the other hand, indicates an underlying process is present causing increased density to lung tissue consistent with alveolar-interstitial syndrome [54-55]. When present bilaterally and diffusely, typically this indicates the presence of pulmonary edema, a diagnosis heightened by the concomitant presence of pleural effusions. The presence and quantity of B lines from suspected pulmonary edema correlates well with an elevated LVEDP [56]. Ultrasound is more sensitive for both pulmonary edema and pleural effusions compared to chest radiography, and is rapidly performed at the bedside [54,55]. However, lung ultrasound also has its limitations as the presence the presence of B-lines does not always correlate with increased extra-vascular lung water and could be related to pneumonia, ARDS, or pulmonary fibrosis.

Abdominal Ultrasound – Venous System

It is critical to identify the presence of volume overload and venous congestion not only in patients with heart failure or cardiogenic shock, but in all forms of pathology. As volume reaches the upper limits of systemic venous capacitance, venous pressure will rise causing congestive changes that can be visualized on ultrasound of the IVC, portal vein, hepatic veins, and the interlobar renal veins [57-60].

Hepatic Vein

Given the multivariate etiologies for its morphology and respirophasic behavior, other venous waveforms should be assessed in conjunction with the IVC to identify venous hypertension and congestion. The hepatic vein will be thin-walled and branch off of the IVC. It can be evaluated from the right coronal plane in long axis view with the pulsed-wave Doppler gate placed perpendicular to the flow to obtain a waveform. Alternatively, the hepatic vein can be obtained anteriorly with the IVC in short axis. In the absence of pathology, there should be an anterograde S and D wave (Figure 6). There is an initial retrograde a wave generated by increased RAP from atrial contraction at end diastole, which is followed by an anterograde S wave caused by decreasing RAP during early mid-systole. If the tricuspid valve is open, however, retrograde deflection can occur causing reversal of the S wave, as seen with tricuspid regurgitation or significant venous congestion. The final D wave is an anterograde deflection caused by decreasing RAP from rapid early diastolic right ventricular filling. With increasing venous congestion, there is a spectrum of waveform changes that occur. The S wave is typically larger, however, with increased RAP and mild congestion, the D wave becomes deeper than the S wave, and with severe congestion, there will be reversal of flow with a retrograde S wave (Figure 6).

Portal Vein

In contrast to the hepatic veins, the portal vein and its branches will have thicker, echogenic walls and will have flow directed towards the transducer. The portal vein should be assessed for pulsatility. Normally the portal vein should have only mild respirophasic variation and should be fairly uniform. With increasing congestion and right atrial pressure elevation, however, the cyclical pressure changes in the right atrium from cardiac contractility get transmitted to the portal circulation creating a pulsatile flow pattern. Once severe congestion is present, the flow form may become biphasic with a sinusoidal retrograde and anterograde flow pattern (Figure 6). The pulsatility index can be measured as follows where normal PI is less than 30% and significant venous congestion is present with a PI >50%:

PI (%) = 100 x [(maximum velocity – minimum velocity)/ maximum velocity]

There have been several studies looking at portal vein pulsatility in patients with congestive heart failure and following cardiac surgery. In one study, of the patients who had portal flow pulsatility, over 60% developed an AKI in the week following surgery [59].

Interlobar Renal Veins

The interlobar renal veins can also be assessed for the presence of venous congestion. Studies looking at ultrasound findings of venous congestion in patients with congestive heart failure have shown that portal vein pulsatility was also associated with alterations of intrarenal venous flow [59,60].

After obtaining a view of the kidney, color Doppler should be placed over the corticomedullary junction to pick up flow through the interlobar vessels with the pulsed-wave Doppler gate placed at the corticomedullary junction ideally obtaining both arterial and venous waveforms. The resistive index can be calculated from the arterial waveform and the venous waveform morphology can also be assessed. Venous flow should be monophasic and continuous, however, with increasing congestion will become pulsatile throughout the cardiac cycle, and with

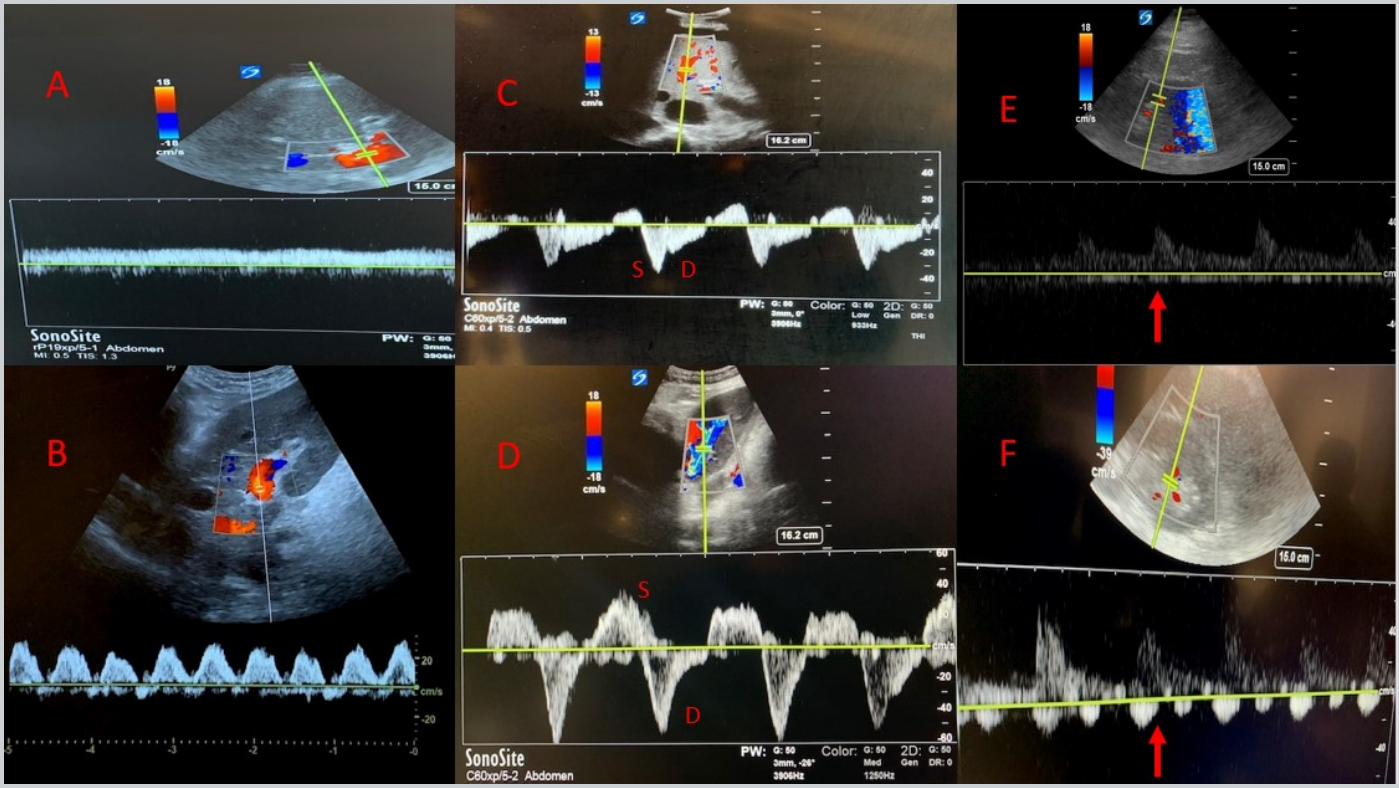

Figure 6. A) Portal vein doppler showing a continuous flow pattern consistent with a normal RAP, B) Portal vein doppler showing biphasic flow consistent with elevated RAP, C) Hepatic vein Doppler showing anterograde S and D wave consistent with a normal RAP, D) Hepatic vein Doppler showing reversal of flow with retrograde S wave consistent with an elevated RAP, E) Renal vein Doppler showing continuous flow consistent with a normal RAP, F) Renal vein Doppler showing discontinuous flow consistent with an elevated RAP.

severe congestion venous flow will only be present in diastole (Figure 6).

Conclusion

Bedside ultrasound can be used to help delineate etiologies for acute kidney injury and to assist in management. Furthermore, ultrasound should be used daily in the ICU to help prevent renal injury by optimizing volume management throughout a patient's admission. Ultrasound should also be used not only in the initial resuscitation, but to guide de-resuscitation as well. More studies are needed regarding the use of bedside ultrasound to better optimize renal perfusion as well as to systematically guide volume removal by continuous renal replacement therapy.

Disclosures

The authors have no conflicts of interest to declare.

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Review

Role of Point of Care Ultrasonography in Patients with COVID-19 Associated Acute Kidney Injury

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Abstract

The severe acute respiratory virus covariate-2 (SARS CoV-2) that causes Corona Virus Disease 2019 (COVID-19) has affected more than 194 million people worldwide and has attributed to or caused more than 4 million deaths. Acute kidney injury (AKI) is a common complication of COVID-19. Point of care ultrasonography (POCUS) can be a useful tool for the nephrologist. POCUS can be used to elucidate the cause of kidney disease and then also help to manage volume status. Here, we review pearls and pitfalls of using POCUS to manage COVID-19 associated AKI with special attention to kidney, lung, and cardiac ultrasound.

Introduction

The severe acute respiratory virus covariate-2 (SARS CoV-2) that causes COVID-19 has affected more than 194 million people worldwide and has attributed to or caused more than 4 million deaths as of July 26th, 2021 [1]. The reported incidence of acute kidney injury (AKI) among patients with COVID-19 vary. In a cohort of 5,449 hospitalized patients in the United States the incidence was reported as 37% [2]. The outcomes among these patients is reported to be poor with 14% requiring dialysis and 35% ultimately dying. Intravascular volume excess frequently complicates acute kidney injury and has been shown to be a poor prognostic indicator in patients with respiratory failure and this remains true in those with COVID-19 [3, 4].

Point of care ultrasonography (POCUS) of the kidneys, lungs, and heart can be crucial to effectively diagnose and manage hospitalized patients with acute kidney injury and COVID-19. A trained nephrologist with a portable ultrasound can make important contributions without exposing additional staff like transporters or technicians. A recent review of the literature has found that most publications on the role of POCUS in COVID 19 have been limited to case series and opinions [5]. However, some data do exist, and some data may be extrapolated from the general medical literature on POCUS. In order to demonstrate the utility of POCUS in managing COVID-19 associated AKI we will present the hospital course of a hypothetical patient that is based upon a real example.

Mr. R is a 46-year-old man with no medical history who presents to the emergency room with difficulty breathing following 10 days of fever, diarrhea, and cough. He is found to have COVID-19 and a serum creatinine of 2.0 mg/dL (176.84 µmol / L).

The first task for the nephrologist is to differentiate AKI from chronic kidney disease (CKD). Hirsch et al. reported that among patients with COVID-19 and AKI, baseline serum creatinine was known in only 15%. Ultrasound at the point of care can help to differentiate between AKI and CKD. The combined thickness of the cortex and medulla on ultrasound is known as the parenchymal thickness and in normal individuals is up to 1.5 cm [6]. In CKD, the parenchyma will be less than 1.5 cm and the sinus fat will appear to be expanded. Additionally, the presence of simple bilateral cysts can indicate the presence of CKD [7]. In this way, POCUS is a quick and effective tool for making this first, important diagnostic step.

The next question for the nephrologist is whether Mr. R's AKI is attributable to a reversible cause, like urinary obstruction. Classic epidemiological studies of AKI in hospitalized patients estimate that urinary obstruction accounts for 1% of cases of AKI in the hospital and rates among COVID-19 associated AKI are similar [8, 9]. However, urinary obstruction remains an important diagnosis because it is more easily treatable. In the hands of a trained practitioner, POCUS carries a reasonable sensitivity to rule out hydronephrosis [10, 11, 12].

Acute tubular necrosis (ATN) is the most common finding among patients with COVID-19 associated AKI [8]. Even on biopsy series where other pathologic processes were found, all cases were complicated by ATN [13]. Reports on the specificity of ultrasound for diagnosing ATN are outdated. Early reports have suggested that renal

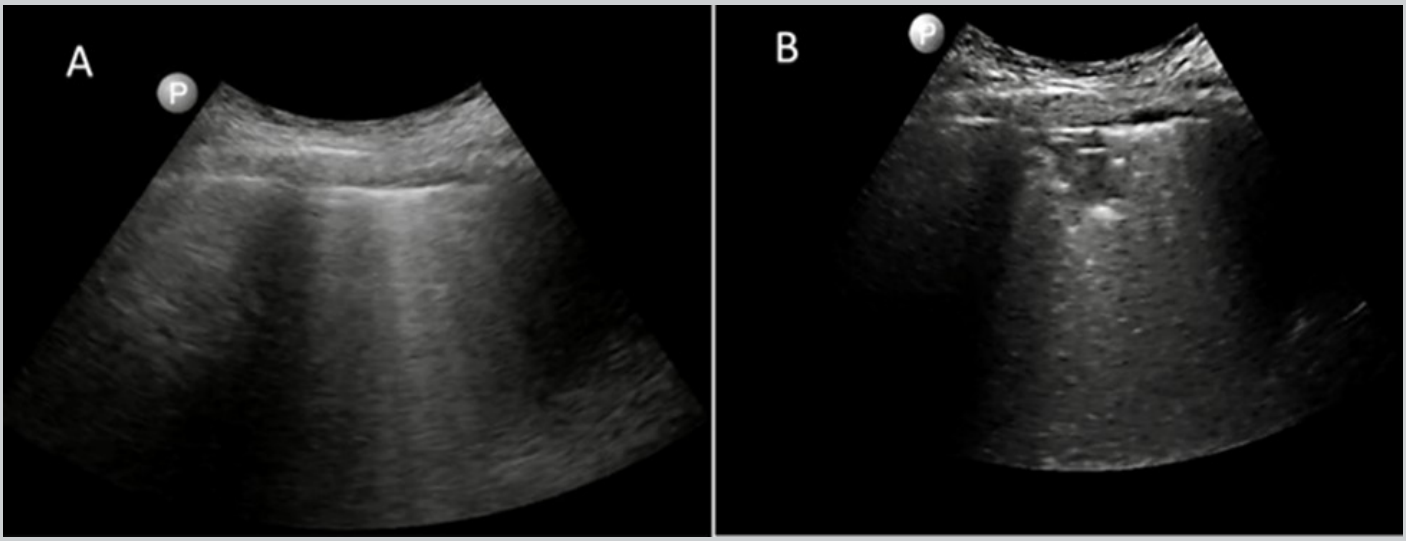

Figure 1. Lung ultrasound images taken using a curvilinear probe (C5 Philips Lumify™) in a patient admitted with COVID-19 pneumonia. Image of an interspace was saved in a six second loop. Both A and B are from the same interspace in the same loop. Image A seems to show B-lines originating from a smooth pleura and could easily be mistaken for pulmonary edema. Image B shows that during the respiratory cycle a subpleural consolidation with trace pleural effusion become evident. This case exemplifies why lung ultrasonography needs to be interpreted with caution when assessing volume status in patients with COVID-19.

ultrasound and Doppler might help with prognostication, but unfortunately, in ATN, kidneys often appear normal [14, 15, 16]. The prevailing opinion is that renal ultrasonography is of limited utility for differentiating ATN from other forms of AKI [17]. It is notable that Doppler waveforms of the venous system are able to accurately identify AKI from venous congestion. The Venous Excess Ultrasound Grading System (VExUS) looks at inferior vena cava (IVC) size along with hepatic, portal, and intra-renal venous waveforms. A congested kidney by these metrics is strongly associated with the development of AKI after cardiac surgery [18].

In summary, urinary obstruction in COVID-19 associated AKI is rare and kidney ultrasonography is of limited utility for diagnosing ATN—the most common form of COVID-19 associated AKI. The most important information clinicians are likely to get from kidney POCUS is differentiating AKI from CKD in an otherwise undifferentiated patient with no known baseline kidney function. Acute kidney injury on CKD in hospitalized patients with COVID-19 is associated with a higher likelihood of requiring dialysis upon discharge [19]. Identifying these patients with kidney POCUS can help nephrologists prognosticate and guide important clinical decisions.

Despite best medical practices, including volume resuscitation, Mr. R gets intubated. He quickly becomes oliguric and his oxygen saturation is dropping.

Is Mr. R's oxygen saturation dropping because he is developing pulmonary edema from renal failure? Or is Mr. R's oxygen saturation dropping because his disease is worsening, and his oliguria is due to days of insensible loss from fever, poor oral intake, and diarrhea? POCUS can be a valuable tool in these scenarios and nephrologists should understand how lung and cardiac ultrasound can be used to augment the traditional physical examination.

Lung Ultrasonography (LUS)

When an ultrasound wave meets a water-thickened interlobular septum, a linear reverberation artifact called a B-line juts away from the pleural surface [20]. In cardiogenic pulmonary edema, these lines will arise from a smooth sliding pleura and will be homogenously distributed both between ribs interspaces and across both hemithoraces [20]. There is an abundance of literature showing that B-lines on LUS correlate with extravascular lung water. In appropriate clinical setting extravascular lung water is associated with cardiac filling pressures. For example, one seminal study by Lichtenstein showed that B-line pattern (diffuse bilateral B-lines) correlates with an elevated pulmonary artery occlusion pressure [21]. In patients with kidney failure on hemodialysis, B-lines are known to disappear in real time with ultrafiltration [22]. In hemodialysis patients, B-lines inversely correlate with ejection fraction and directly correlate with mortality [23, 24].

Lung ultrasonography might be an attractive tool for evaluating extravascular lung water and thereby volume

Figure 2. Inferior vena cava imaged with a curvilinear probe (C5 Philips Lumify™) from a subxiphoid approach.

status in patients with COVID-19 associated AKI. Yet, there are potential pitfalls. It is critically important for the POCUS practitioner to be able to distinguish between lung ultrasound findings consistent with pulmonary edema and those findings consistent with COVID pneumonia. Figure 1 demonstrates typical lung ultrasound findings in COVID-19.

In a case series by Yasukawa in Washington D.C., 10 patients presenting to the emergency department with COVID-19 all had a diffusely irregular pleura, all the patients had areas of confluent B-lines and half also had subpleural consolidations [25]. Subpleural consolidations can be particularly challenging for the novice POCUS practitioner. These consolidations appear as a subtle hypoechoic area directly underneath the pleura. If the ultrasound depth is set incorrectly, it can be easy to mistake these for the septal B-lines of early cardiogenic pulmonary edema.

A case series of 3 physicians with COVID-19 on home isolation showed a typical pattern in mild disease from an irregular pleura with scattered B-lines and subpleural consolidations that progressed to confluent B-lines on day 5 to 7 of illness followed by resolution back to A-line pattern [26]. In a prospective study of 89 patients with severe COVID-19 disease, all patients had B-lines and these were confluent in 78.6%. Similarly, 78.6% of patients had pleural line irregularities in > 6 intercostal regions. Surviving patients were followed at 5 to 6 weeks post discharge and at that time B-lines and irregular pleura were seen in 15.6% [27]. Two reviews that have looked at the reported cases of lung ultrasonographic findings in COVID-19 have come to similar conclusions. COVID-19 pneumonia is often located posteriorly and peripherally. Early findings include a thickened, irregular pleura which progresses to scattered B-lines with subpleural consolidations and then finally result in confluent B-lines. With clinical recovery, there is a return to normal aeration pattern (A-lines) [5, 28]. In the early stages of COVID-19, B-lines might appear to have skip lesions with an irregular pleura making them easy to differentiate from pulmonary edema. However, in the more advanced stages of COVID-19 pneumonia, B-lines become confluent and without careful attention to the pleural line, the findings can be misconstrued. Therefore, it is important to use your high frequency linear probe to analyze the pleura when questions remain. In the appropriate setting and when interpreted correctly, lung ultrasonography can reliably predict COVID-19 in patients with respiratory failure [29].

Focused Echocardiography

Given the high mortality associated with volume overload identifying volume status in patients with COVID-19 associated AKI is critical. Lung ultrasound findings might be unreliable or misleading. This is where using your standard four cardiac views are helpful. The parasternal long axis can be used to look at mitral valve excursion and overall left ventricular function. The parasternal short axis can be used to look for left ventricular contractility and wall motion abnormalities. The apical four chamber view can be used to look for left ventricular and right ventricular size and function comparison, as well as pericardial effusion. The subxiphoid can be used to look at the inferior vena cava (IVC). An early case series from Wuhan, China described three cases where focused cardiac echo was used in patients with COVID-19 to identify new onset global left ventricular dysfunction and acute myocardial infarction [30]. Echocardiography is a versatile tool and can even be used when the patient is in the prone position [31].

Imaging of the inferior vena cava is may be useful in managing critically ill patients with AKI requiring dialysis

and this remains true in COVD-19 [32, 33]. Shamsah et al. performed a prospective observational study of echocardiography in critically patients with COVID-19. In their analysis, they compared 77 patients admitted with COVID-19 who were not mechanically ventilated. They found that upon admission to the ICU, 80% of patients were noted to have an IVC < 2 cm and a collapsibility greater than 50%. The left ventricular ejection fraction of these patients was estimated to be 66% on average. These findings suggest that these patients were intravascular depleted when they entered the ICU. A collapsing IVC in a patient with COVID-19 associated AKI is shown in Figure 2.

Despite best efforts, Mr. R's saturation drops below 80% on 100% FiO2 and therefore he requires extracorporeal membrane oxygenation (ECMO).

Patients with severe COVID-19 pneumonia and severe acute respiratory distress syndrome (ARDS) may remain hypoxemic despite best ventilator practices. These patients may require ECMO for life support if they remain hypoxemic. Depending on the type of failure the patient has, they may require veno-venous (VV) ECMO for primary respiratory failure, or veno-arterial (VA) ECMO for primary cardiac and respiratory failure. According to the worldwide Extracorporeal Life Support Organization registry, of the 2,132 cases of ECMO for COVID-19 reported thus far, 95% (2032) have been for VV-ECMO, reflecting the severe respiratory failure COVID-19 patients experience [34]. There have been reports of COVID-19 related myocarditis, but these remain case reports and case series, so further studies are needed [35]. As ECMO is being used more for COVID-19 support, it is important to recognize how management in these patients differs from other COVID-19 ICU patients. Traditional measurements of hemodynamics are unreliable with ECMO, and therefore POCUS becomes more important.

To understand the role POCUS and transesophageal echocardiography plays in managing patients on ECMO, we must explain the different configurations of ECMO. In VV-ECMO, a large outflow/drainage cannula (21-25 Fr) is placed at the IVC/RA junction, typically via the femoral vein, along with an inflow cannula (17-21 Fr) into the SVC/RA junction. Sometimes femoral vein to femoral vein configurations are used and so it is important to know which configuration your patient has [36]. These cannulas are inserted percutaneously or via cut down by the intensivist or cardiothoracic surgeon. Insertions are guided by fluoroscopy, or by echocardiography by visualizing the insertion of the guidewire into the IVC by utilizing a traditional subcostal view on ultrasound. VA-ECMO requires fluoroscopy and transesophageal echocardiography for insertion, with the inflow cannula sitting in the femoral artery at the level of the common iliac artery.

POCUS is helpful in managing ECMO patients purely from a circuitry standpoint. For both VV- and VA-ECMO patients, POCUS helps identify atrial and ventricular size and function, valvular regurgitation, thrombus, the presence of pericardial effusion, and, most importantly, cannula position [37]. A mispositioned ECMO cannula, either the drainage or inflow cannula, may result in sub-optimal ECMO function, and ultimately, patient hypoxemia and hypoxia [38]. While on ECMO, special consideration must be given to the patient's volume status, as it can affect the flows on the ECMO circuit.

Nephrologists who use POCUS need to be aware of the limitations of interpreting IVC size and variability in patients on ECMO. The drainage cannula often sits in the IVC. This catheter can be anywhere from 21-25 Fr, meaning as much as 8.33 mm in diameter. Drainage cannulas are typically multi-stage cannulas, meaning they are perforated on the edges to allow for maximal drainage of the IVC. Therefore, the IVC must remain larger than the cannula diameter in order to ensure continuous, uninterrupted flow for the ECMO circuit [37]. The IVC and drainage cannula can be seen in the subcostal view using POCUS. If the IVC appears to be collapsed around the cannula, the nephrologist and intensivist must exercise caution in further fluid removal, and in fact may need to give the patient fluid, in order to prevent "chattering" on the ECMO circuit, resulting in fluctuating flows and ultimately, hypoxemia.

Sometimes, the cannulas may not be visualized using transthoracic echocardiography. These patients may need transesophageal echocardiography (TEE) to see if the cannulas are positioned appropriately. Transesophageal echocardiography can also be used to elucidate the cause of hypoxemia. Both trans-thoracic and trans-esophageal echocardiograms can be used to identify a right to left intra-cardiac shunt, such as due to a patent foramen ovale, that might explain a patient's hypoxemia. Transesophageal lung ultrasound (TELUS) is increasingly recognized as a tool to diagnose hypoxemia in patients who are too critically ill to move to a CT scanner and in whom other traditional imaging modalities are not practical or safe [38]. TELUS can show lung consolidations at the bases in obese patients and whether there are A-lines, B-lines, irregular pleura, or pleural effusions. TEE can identify a thrombus in the pulmonary artery, a dilated right ventricle, or impaired left ventricular contractility [38] TELUS can also help determine whether the patient's hypoxemia can improve with recruitment maneuvers, or if there is a volume issue at play.

Table 1. Point of Care Ultrasonography in COVID-19 Associated Acute Kidney Injury -- Key Points

Kidney and Bladder Ultrasound	• Urinary obstruction is an uncommon but reversible cause of AKI • Many patients have no known baseline creatinine and so POCUS is useful to identify CKD.
Lung Ultrasonography	• Confluent B-lines are common • Irregular pleura is common • Sub-pleural consolidations are common • Careful attention to the pleural line is needed for accurate interpretation
Echocardiography	• Many patients have collapsible IVC and hyperdynamic LV prior to intubation • When patients are on ECMO, TTE and TEE is useful for evaluating lungs and cardiac chambers, as well as cannula position. It can inform when not to remove fluid because of ECMO considerations.

While on ECMO, Mr. R required intermittent boluses of colloid due to fluctuating ECMO flows and an IVC collapsed around his drainage cannula, even though he clinically appeared euvolemic. POCUS showed improved aeration of his lung bases and anterior lung fields. He was able to be weaned off VV-ECMO. His IVC appeared dilated with no respiratory variation post-VV-ECMO, and fluid was restricted. His acute kidney injury resolved, and urine output improved.

Conclusion

Point of care ultrasonography has a variety of uses for the nephrologist evaluating COVID-19 associated AKI (Table 1). A nephrologist well trained in ultrasound can minimize exposure from additional staff such as technicians and patient transporters that are required for formal radiology studies. Kidney ultrasound can help identify obstruction and CKD. Many patients during the pandemic arrive with no known baseline kidney function. Chronic kidney disease is associated with a higher mortality and higher likelihood of requiring dialysis upon discharge. Therefore, POCUS can give the nephrologist important prognostic information. Ultrasound-based volume assessment is important in managing hypervolemia. Lung ultrasonography needs to be interpreted with caution because B-lines often arise from an irregular pleura due to the underlying pulmonary process, and can also be seen with subpleural consolidations. When patients require ECMO, TEE and TELUS can be useful for evaluating volume status. As COVID-19 continues to spread across the globe, nephrologists should become more informed about how POCUS can improve the care of their patients.

Disclosures

The authors have no conflicts of interest to disclose.

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Review

Integrative Volume Status Assessment

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Abstract

Volume status assessment is a critical but challenging clinical skill and is especially important for the management of patients in the emergency department, intensive care unit, and dialysis unit where accurate intravascular assessment is necessary to guide appropriate fluid management. Assessment of volume status is subjective and can vary from provider to provider, posing clinical dilemmas. Traditional non-invasive methods of volume assessment include assessment of skin turgor, axillary sweat, peripheral edema, pulmonary crackles, orthostatic vital signs, and jugular venous distension. Invasive assessments of volume status include direct measurement of central venous pressure and pulmonary artery pressures. Each of these has their own limitations, challenges, and pitfalls and were often validated based on small cohorts with questionable comparators. In the past 30 years, the increased availability, progressive miniaturization, and falling price of ultrasound devices has made point of care ultrasound (POCUS) widely available. Emerging evidence base and increased uptake across multiple subspecialities has facilitated the adoption of this technology. POCUS is now widely available, relatively inexpensive, free of ionizing radiation, and can help providers make medical decisions with more precision. POCUS is not intended to replace the physical exam, but rather to complement clinical assessment, guiding providers to give thorough and accurate clinical care to their patients. We should be mindful of the nascent literature supporting the use of POCUS and other limitations as uptake increases among providers and be wary not to use POCUS to substitute clinical judgement, but integrate ultrasonographic findings carefully with history and clinical examination.

Introduction

Assessment and early optimization of volume status are integral parts of the medical care of critically ill patients especially patients with heart failure, acute kidney injury, and end stage kidney disease (ESKD) on dialysis [1]. Decisions on the administration of diuretics, initiation of renal replacement therapy, and ultrafiltration goals rely on proper intravascular assessment. Often, however, in absence of a gold standard, providers' volume assessments and decisions are not straightforward. For centuries, physicians have relied on the patient's history and clinical examination findings to come to a differential diagnosis and the most plausible explanation. Yet the accuracy and precision of clinical examination findings are often based on methodologically flawed studies with limitations including small sample size, questionable comparators, and limited generalizability. Thorough clinical examination findings, though important, are often subjective and can lead to bias in decision making process. As the medical field makes progress toward precision medicine, physical examination findings have been supplemented with imaging as well as and invasive modalities such as central venous pressure (CVP) and pulmonary artery (PA) catheter wedge pressure monitoring. More recently, point of care ultrasound (POCUS) examination at bedside has come into widespread practice and has become a fifth pillar of clinical medicine [2]. In this review, we discuss integration of conventional methods with newer point of care ultrasound tools for accurate volume assessment during routine care.

Conventional Methods of Volume Assessment and Pitfalls

Traditionally, volume status assessment rested on history and physical examination. These methods are readily available, cheap, simple, and non-invasive to the patient and are indispensable in the present time. Even in the era of POCUS, history and physical examination are the clinicians' first steps in assessing volume status.

Mucus Membrane Examination

Mucus membranes of the tongue and oral mucosa are dry in dehydration and intravascular volume depletion. Tongue dryness ($P < 0.001$) and dryness of the mucous membranes of the mouth ($P < 0.001$) correlated with severity of dehydration independent of age [3]. Dry oral mucosae were associated with hypernatremia (OR = 10.46, 95% CI 6.04 - 18.09) in one case control study [4]. Moist mucus membranes and engorged sublingual veins can be present in the context of intravascular volume overload.

Capillary Refill Time

Capillary refill time is determined by compressing the distal phalanx of the patient's middle finger positioned level with the heart for 5 seconds and then timing the return of normal color to the finger. The normal capillary refill times are 2 seconds for children and adult men, 3

seconds for adult women, and 4 seconds for the elderly [5,6]. The capillary refill time is also dependent on ambient temperature. Prolonged refill time does not accurately predict hypovolemia (6% sensitivity and 93% specificity) and yields a positive LR of 1.0 [7].

Skin Turgor and Axillary Sweat Examination

Poor skin turgor refers to the slow return of skin to its normal position after being deformed. This can be assessed clinically by pinching the skin between the examiner's thumb and forefinger [8]. In a clinical study enrolling elderly patients presenting to emergency departments with vomiting, diarrhea, and/or decreased oral intake presence of dry axilla was only 50% sensitive and 82% specific with a likelihood ratio (LR) of 2.8 for hypovolemia [4]. Abnormal skin turgor in the subclavicular area (presence of skin tenting for 3 or more seconds after 3 or more seconds of pinching) was 73% sensitive and 79% specific with a LR of 3.5 for hypovolemia if present [4]. The protein elastin, which is responsible for skin recoil, deteriorates with age, limiting the specificity of this test in patients with advanced age [4].

Orthostatic Vital Signs

Orthostatic vital signs remain a useful bedside tool to aid in the assessment of volume status. When obtaining postural vital signs, clinicians should wait two minutes before measuring the supine vital signs and one minute after standing before measuring the upright vital signs [5]. Orthostatic hypotension is defined as a decrement in systolic blood pressure (SBP) of > 20 mmHg after standing from the supine position [5]. In a study of pregnant women presenting to the ED with hyperemesis gravidarum, a 20 mmHg drop in SBP was only 29% sensitive and 81% specific for identifying hypovolemia [9]. A drop in SBP by 20 was only 9% sensitive in younger than 65 years and 27% in older than 65 years for detecting moderate blood loss (450-630 ml) [5]. The limitation is that orthostatic hypotension has many additional causes beyond volume depletion. This holds particularly true in elderly patients, but also those on vasodilatory agents, those on anti-depressants, and those with a primary autonomic dysfunction like Parkinson's Disease.

Jugular Venous Pressure Measurements

Jugular venous pressure (JVP) is measured with patient lying with head of bed at 30-45 degrees with head turned 30-60 degrees away from examiner. The elevation of the neck veins above the sternal angle vertically is measured using tangential light and 5 cm added (right atrium [RA] is 5 cm below the sternal angle) [10,11]. While subject to error, JVP measurements are frequently used for assessment of intravascular volume. In studies comparing JVP measurement to pulmonary artery (PA) catheter measurements, bedside measurements of JVP were within 4 cm of water of the catheter-based measurements 85% on the time [12]. Furthermore, a JVP measurement greater than 8 cm of water carries a sensitivity between 47-92%, and a specificity of 93-96% with a positive LR of 9.7 for an elevated central venous pressure (CVP). Conversely, if the measured JVP is less than 5 cm H_20, this carries a 90% sensitivity, 89% specificity, and positive likelihood ratio (LR) of 8.4 for a low CVP [12,13]. An additional provocative maneuver, namely testing for hepatojugular reflux, carries a positive LR of 8 for an elevated CVP if positive [14,15].

JVP measurement is still fraught with problems. The failure to accurately visualize the JVP by physical examination ranges from 10% to 80% [11,16]. Morbid obesity and a wide neck circumference preclude the internal jugular (IJ) vein from being visualized altogether. An inexperienced operator can frequently misidentify external jugular (EJ) vein for the IJ vein or carotid artery for the IJ vein. Excessive extension or rotation of the chin tenses the sternocleidomastoid muscle leading to compression of the IJ vein and inability to identify this structure. Atrial fibrillation and tricuspid regurgitation can cause the IJ vein to be mistaken for the carotid artery [17].

Edema

Peripheral edema is a frequent sign encountered clinically and provides information about interstitial volume. Unfortunately, its presence lacks sensitivity and specificity for the intravascular volume, as numerous disease states can cause edema. These include disease states with increased capillary hydrostatic pressure including volume overload and deep venous thrombosis, but also decreased capillary oncotic pressure as in hypoalbuminemia, increased interstitial hydrostatic pressure as in lymphatic obstruction, and increased capillary permeability as in cellulitis. Therefore, peripheral edema suggests hypervolemia when accompanied by other signs of elevated filling pressures, but in isolation its low sensitivity lacks usefulness [18]. The presence of peripheral edema does not necessarily indicate fluid overload and these patients can still be intravascularly depleted or euvolemic [19]. In fact, among patients with ESKD, pedal edema correlated with age, body mass index, and left ventricular mass, but did not reflect intravascular volume status [20].

Lung Examination and Chest Radiograph

Presence of bilateral crackles and rhonchi is suggestive of pulmonary edema [21]. Dull percussion is associated with pleural effusion. Pleural effusions indicate increase third space volume. However, for auscultation, the

sensitivity is 51% (43-60%), specificity is 79 % (73-84), diagnostic accuracy is 69% (64-74%) for detection of alveolar-pulmonary edema [22].

Chest x-rays (CXR) are frequently used for assessment of pulmonary vascular status (alveolar edema) characterized by prominent pulmonary veins. The decision in the use of diuretics is commonly made by the presence of alveolar edema on CXR. In a study of 500 chest x-rays in 200 ICUs, CXR findings led to change in therapy in 66% of patients [23]. Another less widespread method has been use of upright posteroanterior CXR in describing the relationship of the vascular pedicle width (VPW) and cardiothoracic ratio (CTR) to diagnose cause of pulmonary edema, limited by inability to obtain such view in critically ill ICU patient [24].

Biomarkers

B-type natriuretic peptide (BNP) and N-terminal prohormone of BNP (NT-proBNP) has been traditionally used as biomarkers for volume overload or heart failure. At levels < 50 pg/ml, BNP had a negative predictive value of 96% and the diagnostic accuracy for a cutoff of 100 pg/mL was 83.4% [25]. Elevated BNP does not always indicate volume overload. Heart failure patients with renal impairment and patients on dialysis have higher concentrations of BNP and NT-proBNP [26]. NT-proBNP value cut off 1200 pg/mL for subjects with GFR < 60 ml/ min/1.73 m^2 had sensitivity and specificity to be 89% and 72%, respectively for detecting acute decompensated heart failure [27]. On the other hand, BNP testing yielded false negative results in 20% of obese heart failure patients when using the clinical threshold of 100 pg/mL [28]. Recent studies have shown serum carbohydrate antigen 125 (CA-125) levels have been associated with state of volume overload and heart failure independently and in combination with NT-proBNP [29-31].

Invasive Methods

Central Venous Pressure (CVP) Measurement

Assessment of CVP is widely available in the intensive care units and is feasible. However, the CVP alone has poor predictive value for fluid responsiveness. A low CVP (mean threshold <8 mm Hg) was associated with fluid responsiveness (positive LR 2.6, 95% CI 1.4-4.6, pooled specificity 76%), but a CVP greater than the threshold made fluid responsiveness less likely (negative LR 0.50, 95% CI 0.39-0.65, pooled sensitivity 62%) [32]. A systematic review demonstrated a poor relationship between CVP and blood volume (pooled correlation coefficient 0.16, 95% CI 0.03 - 0.28) and was unable to predict the hemodynamic response to a fluid challenge [33]. Several technical aspects of the measurement related to zeroing and leveling of the measuring device can lead to inaccurate measurement of the preload value [34].

Pulmonary Artery Catheter Pressures

While routine use of pulmonary artery catheter (PAC) has fallen out of favor in the intensive care units (ICU), it is still useful in understanding a patient's hemodynamics. In one small study, when compared with a physician's prediction of a variety of hemodynamic variables, PACs were vastly superior. Predictions of RA pressure were accurate approximately 50% of the time [35]. However, PAC did not affect overall mortality (OR 1.26; 95% CI, 0.78-2.03; P = 0.35) and hospitalization (HR 1.04, 95% CI 0.86-1.27, P =0.67. Based on the ESCAPE trial, PACs are not routinely indicated to adjust therapy during hospitalization for decompensation of chronic heart failure [36].

Transpulmonary Thermodilution and Pulse Contour Analysis

Transpulmonary thermodilution (TPTD) and pulse contour analysis are invasive and advanced hemodynamic monitoring techniques used for measurement of cardiac index (CI) and the assessment of cardiac preload by measuring dynamic cardiac preload variable volume variation (SVV) which helps in assessing responsiveness to fluid and pulmonary vascular status. These can be measured accurately only in sinus rhythm and controlled ventilation [37-39]. The TPTD technique provides the variable extravascular lung water index (EVLWI) for the assessment of pulmonary hydration [39,40]. The details of these methods are beyond the scope of this review. These methods are invasive, expensive, and not widely available.

Point of Care Ultrasound for Volume Assessment

Point of Care Ultrasound (POCUS) is a bedside ultrasound examination performed by the clinician to answer a focused clinical question. Widespread use of POCUS in the last decade has been shown to improve diagnostic accuracy when used simultaneously with clinical examination [22,41]. Here we describe methods of volume assessment using POCUS as well as their limitations.

1. Internal Jugular Vein Assessment

Ultrasonography of the internal jugular (IJ) vein has been used in the estimation of CVP. The IJ is first identified in transverse section using the linear probe and then the probe is rotated 90 degrees cranially with indicator to the patient's head. Image of IJ is obtained where IJ narrows into a paintbrush appearance (Figure 1). The height where the IJ tapers correlates with jugular venous distension [42]. The IJ diameter is measured using M-mode through several respiratory cycles, and the end expiratory diameter is used as the final measurement. In

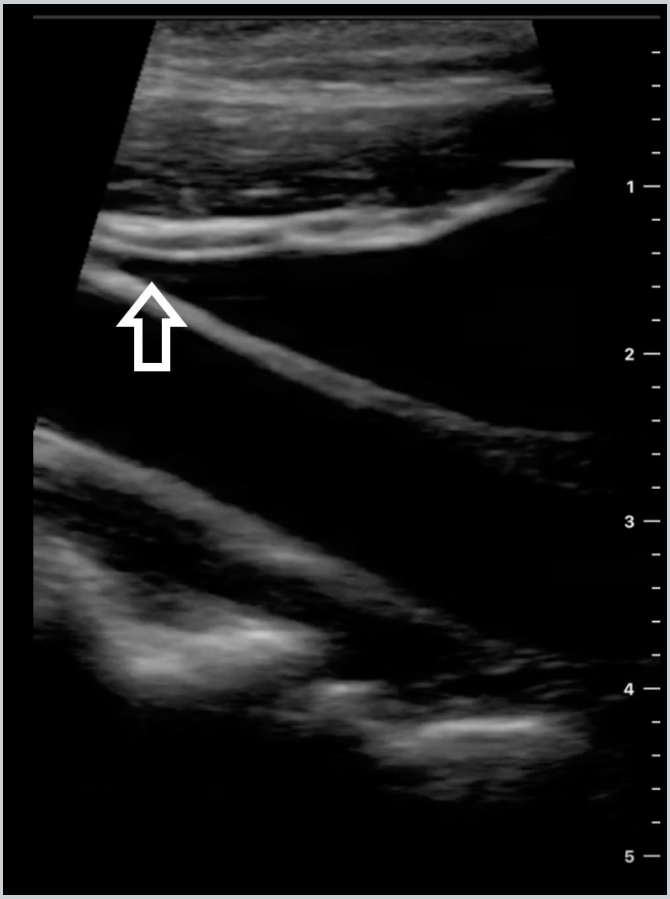

Figure 1. Internal jugular vein showing paint brush sign (arrow).

a small study of non-ventilated patients who were simultaneously undergoing CVP monitoring, a mean IJ vein diameter of 7 mm correlated with a CVP <10 mmHg (95% CI, 5.7-8.3), whereas the IJ vein diameter on 12.5 mm correlated with CVP >10 mmHg (95% CI, 11.2-13.8) [43]. Being able to distinguish the IJ vein from the carotid artery is essential to avoid pitfalls.

2. Inferior Vena Cava Assessment

Inferior Vena Cava (IVC) measurement is a commonly used ultrasound technique for estimating volume status. To measure IVC, a curvilinear or cardiac probe is placed in the subxiphoid space with transducer flat against the abdomen identifying RA and gradually fanning the probe until the intrahepatic IVC can be identified. The probe is then rotated 90 degrees to obtain the IVC in long axis view. IVC diameter is measured 2 cm inferior to the cavoatrial junction or about 1 cm inferior to the branching of the hepatic veins (Figure 2) [42,44]. M-mode can be used to track IVC collapse during inspiration in spontaneously breathing patients [42].

Measurements used are IVC diameter and caval index or collapsibility index which is calculated as expiratory IVC diameter (IVC_{max}) minus inspiratory IVC diameter (IVC_{min}) all divided by IVC_{max} $\left(\frac{IVC_{max}-IVC_{min}}{IVC_{max}}\right)$ [42]. When compared with PA catheter measurements, a caval index ≥ 50% indicates RA pressure <10 mm Hg, and caval index <50% indicate RA pressure ≥10 mmHg [45]. In a study of outpatient hemodialysis patients, 2 kg weight reductions after hemodialysis were associated with a >10% change in caval index [46]. In a study including 39 mechanically ventilated patients with septic shock, 12% respiratory variation calculated as the difference between the maximum and the minimum diameter, normalized by the mean of the two values was associated with an increase of cardiac output after fluid resuscitation [47].

The pooled sensitivity and specificity for an IVC ultrasound as a predictor of fluid responsiveness were 0.63 (95% CI 0.56-0.69) and 0.73 (95% CI 0.67-0.78) respectively with a pooled area under the receiver operating characteristic curve of 0.79 (standard error 0.05) [48].

There are many pitfalls when examining the IVC. The abdominal aorta is frequently mistaken for the IVC by inexperienced examiners. IVC and aorta are best distinguished by noting the hepatic veins joining the IVC and the intrahepatic course of the IVC [42]. Severe tricuspid regurgitation, tricuspid stenosis, massive pulmonary embolism, cardiac tamponade, restrictive and constrictive cardiomyopathy, pulmonary hypertension, impaired IVC drainage to heart, IVC thrombosis, congestive heart failure, impaired right atrial filling and positive pressure ventilation are commonly encountered scenarios which can lead to a low caval index [49,50]. Changes in intrabdominal pressure, changes in tidal volume on mechanical ventilation, thrombosis of IVC, and presence of an IVC filter are some factors that can affect the IVC diameter and changes seen with inspiration [19]. Sometimes patients are unable to tolerate a probe over the subxiphoid space due to

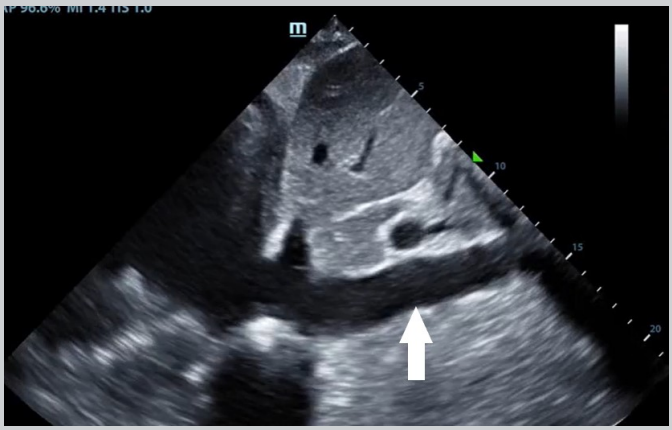

Figure 2. Inferior vena cava. This is subxiphoid view obtained with a linear probe placed below the xiphoid process (white arrow indicating dilated IVC).

abdominal pain or after major abdominal surgeries. The most common error in IVC assessment is failure to identify a slit-like IVC when it is underfilled [42].

3. Lung Ultrasound

The volume assessment using lung ultrasonography (LUS) involves examining the patient for B-lines. To evaluate for B-lines, linear probe is used in a vertical configuration placed over the intercostal spaces in the mid-clavicular and mid-axillary lines. B-lines are hyperechoic vertical lines extending from the pleura down to the bottom of the US image (Figure 3). Two or fewer B-lines in each section is considered normal. Alveolar-interstitial syndrome was defined as the presence of more than 3 B-lines or "white lung" appearance for each examined area. Lung pulse was defined as the absence of lung sliding at the pleural line [51].

A meta-analysis showed that LUS is 88% sensitive and 90% specific for acutely decompensated heart failure and was more sensitive at detecting pulmonary edema than CXR [52]. LUS B-lines have a high interobserver reliability (concordance index = 0.96) in patients on hemodialysis [53]. In dialysis patients, B-lines might be an early marker of extravascular lung water and are likely present before clinical symptoms of dyspnea appear [54]. Thirty-four of 40 patients had statistically significant reductions in the number of B-lines from pre-dialysis to the midpoint scan and from pre-dialysis to post-dialysis with a P value < 0.001 [54]. Patients with an ejection fraction < 50% had pre-dialysis B lines of 45 ± 37; those with ejection fractions > 50% had pre-dialysis B lines of 18 ± 17 [54]. In the Lung Water by Ultra-Sound Guided Treatment to Prevent Death and Cardiovascular Complications in High Risk ESRD Patients with Cardiomyopathy (LUST) trial, the median number of LUS B-lines before a regular hemodialysis session was 9, and the inter quartile range spanned from 5 to 19 lines [55], estimating to median accumulation of water in the lungs of about 1.2 L in a range comprised between 0.5 and about 2.2 L [56]. The number of LUS B-lines decreased in 79% of patients after dialysis and did not change in

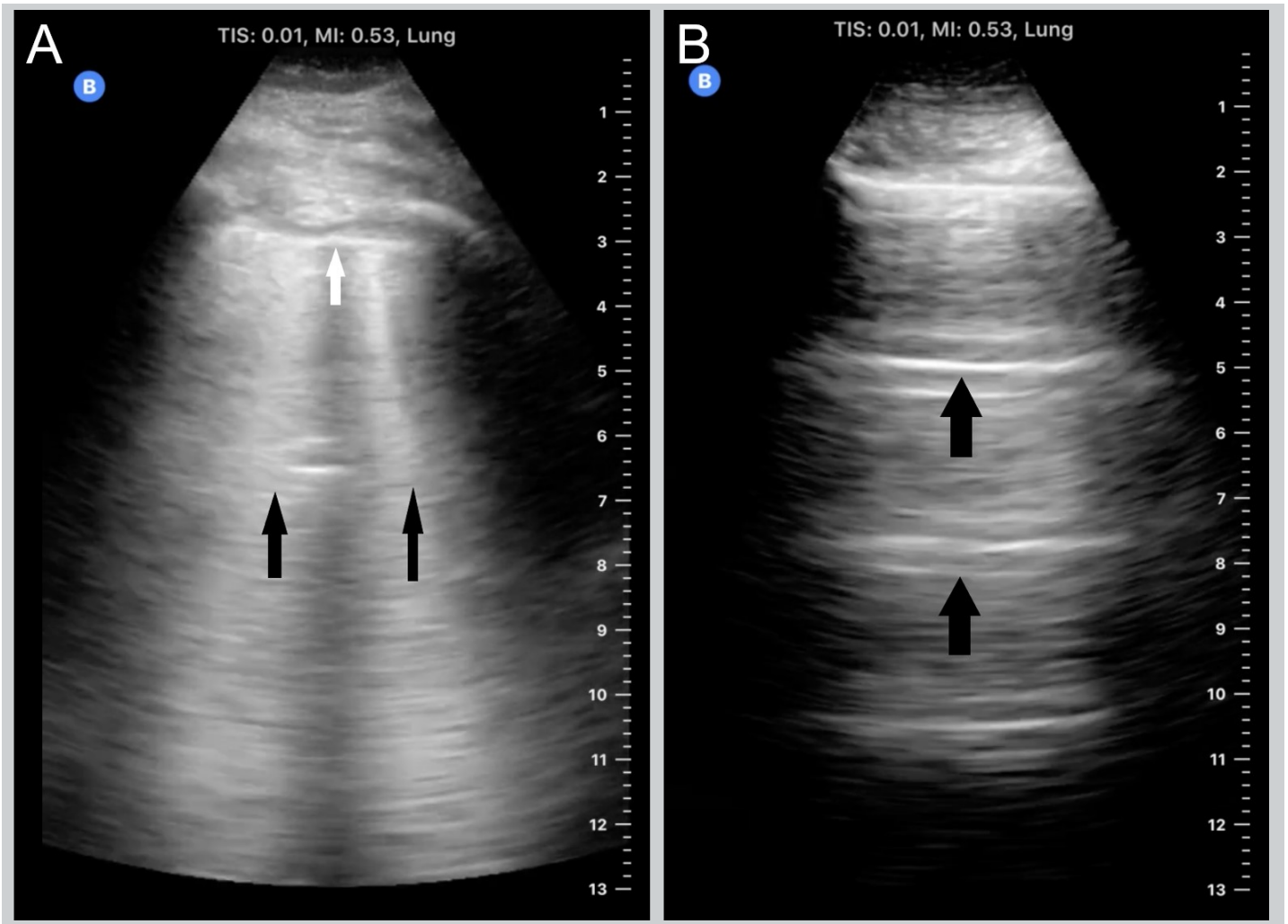

Figure 3. Lung US. A) demonstrating B lines (black arrows) and pleural line (white arrow). B) demonstrating A lines (black arrows)

21% of patients (i.e., remained exactly the same or changed by two US-B lines at most) [55].

While heart failure is one of many causes of pleural effusions, pleural ultrasound remains a useful tool in assessing volume status. Pleural effusions are easily visualized with a bedside ultrasound by placing a curvilinear probe in the midaxillary line. Pleural effusion can also be detected in cardiac views. Characteristically, left-sided pleural effusion appears posterior and lateral to the descending aorta in parasternal long axis view (PLAX) and apical 4-chamber views (A4C) [57-59]. In subcostal views, a right pleural effusion can also be visualized besides the right cardiac chambers, extending over the bare area of the liver [59].

A meta-analysis determined the sensitivity and specificity of ultrasound for detection pleural effusions as 93% (95% CI, 89% - 96%) and 96% (95% CI, 95% - 98%), respectively [60]. The sensitivity approaches 100% with pleural effusions >100 mL in volume.

However, isolated LUS will not be adequate to make diagnosis of pulmonary edema as the LUS findings can been seen in acute respiratory distress syndrome (ARDS), chronic interstitial lung disease, pneumonia, or other inflammatory conditions which may be difficult to distinguish from that of cardiogenic pulmonary edema [19]. The presence of heterogenous distribution of B-lines with spared areas of normal lung in the anterior lung field and homogenous compact B-lines giving appearance of white lung and consolidations with air bronchograms in the posterior lung, reduced lung sliding, and irregular or thickened pleural lines is suggestive of ARDS/pneumonia while homogenous B-lines in anterior and posterior lung fields with absence of pleural irregularity/thickening are consistent with cardiogenic pulmonary edema [51,61]. Patient positioning may also limit from obtaining adequate lung scan zones for comprehensive evaluation [19].

4. Focused Cardiac Ultrasound

Focused cardiac ultrasound (FoCUS) can provide a vast amount of data which can be used to interpret volume status. FoCUS allows for rapid evaluation of the "five Es:" pericardial **e**ffusion, qualitative assessment of left ventricular **e**jection, right and left ventricular **e**quality (e.g., right ventricle enlarges due to pulmonary hypertension or embolism), **e**xit (aortic root diameter), and **e**ntrance (IVC) [62].

FoCUS involves PLAX, a parasternal short axis (PSSA), an A4C, and a subcostal 4 chamber or subxiphoid view [62]. PLAX view is obtained by placing probe along the left sternal border at 2nd to 4th intercostal space, perpendicular to the patient's chest with the probe index marker angled toward the patient's right shoulder and PSSA view by rotating the probe 90 degrees with index toward the left shoulder [44,50,63]. PLAX view allows visualization of left atrium (LA), mitral valve (MV), left ventricle (LV), aortic valve, right ventricle (RV), pericardium, and descending aortic root (Figure 4) [44]. A4C view is obtained with the transducer near the apex of the heart at the point of maximal impulse and directing the index marker toward the patient's left shoulder to obtain a simultaneous view of the LV, the RV, the LA, the RA, the MV, and the tricuspid valve [50]. Subxiphoid or subcostal 4-chamber view is obtained by placing the probe in subxiphoid area as described above during IVC assessment [50].

Pericardial effusion is seen in several different focused cardiac views, but subxiphoid view provides the clearest and most reliable image [50,62]. In the PLAX and PSSA view, significant effusions are visualized posterior to the LV and anterior to descending aorta and in the A4C view,

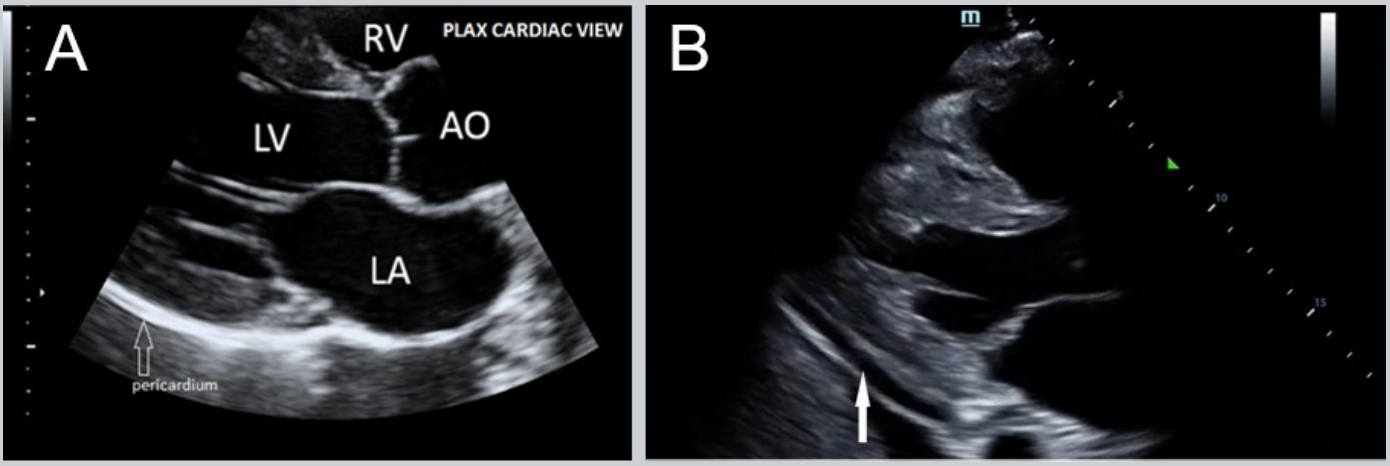

Figure 4. A) Focused cardiac ultrasound (FoCUS). Parasternal long axis view (PLAX) showing different chambers and aorta. B) Focused Cardiac Ultrasound. PLAX view showing pericardial effusion (white arrow).

small effusions are visible lateral to the LV free wall, while moderate to large effusions may be seen around the apex of the heart [62]. Small effusions are smaller than 1 cm, moderate effusions are 1 to 2 cm, and large effusions are >2 cm [62,64]. Findings suggestive of cardiac tamponade include, in sequence, collapse of the RA followed by collapse of the RV, and finally LV collapse [65], accompanied by plethoric non collapsible IVC (fifth "e" described above) [62,66]. POCUS was able to demonstrate pericardial effusion with a sensitivity of 96% and a specificity of 98% in emergency room [67]. A common pitfall of assessment of pericardial effusion in US is mistaking epicardial or pericardial fat for pericardial effusion [68].

LV ejection fraction (LVEF) is estimated by qualitative assessment for evaluation for cause for hypotension, chest pain, and dyspnea [62]. LVEF can be estimated using PLAX view by the MV E-point septal separation method (EPSS) with visual assessment or measurement of smallest distance between anterior MV and the interventricular septum. Movement to within 1 cm of the septum suggests that the LVEF is likely preserved [44,50,62,63,69,70]. In PSSA view, concentric LV squeeze can be observed by estimating the degree of internal chamber collapse in systole versus diastole [62]. A severely depressed ejection fraction, when combined with a plethoric IVC (and/or B-lines), indicates systolic heart failure [62]. Pitfalls include presence of septal hypertrophy, mitral stenosis, atrial fibrillation, and mismeasurement [62].

Quantitative assessments can also be done in FoCUS for volume assessment. LV internal diameter at the end of diastole (LVIDD) is measured in the PLAX view with the diameter 1 cm distal to the MV annulus in M-mode (reference ranges for LVIDD 3.9 to 5.3 cm in women and 4.2 to 5.9 cm in men); smaller diameters are suggestive of hypovolemia [71]. LV end-diastolic area <10 cm^2 is suggestive of hypovolemia and > 20 cm^2 indicates volume overload. It is important to note that LV hypertrophy can cause a low LVIDD and therefore lead to erroneous assumptions of volume status [72]. Doppler transmitral flow can also be obtained with POCUS and is related to LV filling patterns [73]. Interpretation of transmitral flow patterns are confounded by mitral and aortic valve disease and are outside the scope of this article.

The relative size of RV and LV (equality) can be assessed best in PSSA view at the level of papillary muscle where the septal flattening, resulting in the characteristic "D-shaped" LV suggestive of elevated RV pressure can be visualized in RV pressure overload. The normal RV:LV diameter ratio is <0.6:1. Acute RV dilation with or without RV hypokinesis can be seen in pulmonary embolism and also helps predict severity [62]. The tricuspid annular plane systolic excursion (TAPSE) is used for estimating the right ventricular systolic function and is best demonstrated in A4C view [62,74]. The TAPSE is obtained by putting the M-mode cursor along the lateral part of the tricuspid valve ring. A TAPSE of 18 mm or greater is typically considered normal [75]. The area under the curve of the TAPSE for the detection of CVP greater than 8 mmHg was 0.860 (95% CI 0.730–0.991, P = .001). TAPSE has the potential to predict the CVP in low LVEF patients and provides a noninvasive way to assess the right atrial pressure [74]. One of the common pitfalls of RV assessment is overestimation of RV:LV ratio due to the ultrasound plane cutting through the RV in an oblique plane that makes the RV look relatively larger than the LV [62].

The fourth "E" mentioned above is used for the assessment of the aortic root for thoracic aortic aneurysm and thoracic aortic dissection (exit from the heart) [62]. Their description is beyond the scope of this review as this is not pertinent to nephrologist for evaluation of volume status.

5. Doppler Ultrasonography

Doppler ultrasonography evaluation of blood flow pattern in hepatic, portal, and intrarenal veins provides an additional tool for assessing volume status and venous congestion in critically ill patients [47]. The probe is placed over the liver in the subcostal position to visualize the middle hepatic vein [76]. Pulsed-wave Doppler is used 2-4 cm from where the hepatic vein drains into the IVC. The waveform of the hepatic vein is reversed with higher velocities seen in diastole in states of volume overload. In severe volume overload, retrograde flow is seen in systole [19].

Moving towards the portal vein, the transducer is placed in the right mid-axillary line [76]. Flow through the portal vein is normally monophasic, but in the presence of hypervolemia, pulsatility will be present. This can be quantified using the pulsatility index $\left(\frac{\max velocity - \min velocity}{\max velocity}\right)$ where a pulsatility index greater than 50% indicates severe volume overload [19,77]. Pulsatility can be seen in cirrhosis in absence of elevated CVP due to arterio-portal shunting [78]. It can also be observed in healthy, thin adults [79].

The intrarenal veins, though small and difficult to visualize, can aid in assessing volume status. The curvilinear transducer is placed on the posterior axillary line. A normal Doppler waveform is continuous. With increasing venous congestion, there is a decrease in the systolic component of the wave with progression to biphasic (systolic/diastolic phases), and with severe renal

congestion, there is complete absence of systolic flow showing only diastolic phase [80].

Using the above Doppler methods, venous excess ultrasound score (VEXUS) scoring system was developed to identify venous congestion that leads to distension of IVC hepatic vein, portal vein, and renal vein abnormalities in acute kidney injury (AKI) due to cardiorenal syndrome [81-83].

Changes in the common carotid artery (CCA) blood flow using Doppler ultrasonography with response to passive leg raise (PLR) has been shown to be an effective tool in predicting fluid responsiveness in hemodynamically unstable patients [84,85]. Passive leg raise (PLR) is a measure of endogenous volume challenge where the fluid shift from lower extremity to intrathoracic compartment increases cardiac preload by redistributing approximately 300–400 mL of blood from the lower extremities to the heart and subsequent improvement in blood pressure [39,86]. An increase of carotid blood flow by 20% after PLR is indicative of fluid responsiveness with a sensitivity of 94% and specificity of 86% [84]. These patients with positive PLR respond to intravenous fluid [86].

We have summarized the sensitivity, specificity, negative predictive values, and positive predictive values of commonly used physical examination and POCUS findings in Table 1.

Integration of Clinical Assessment and POCUS

Conventional physical examination has limited diagnostic utility with poor specificity and sensitivity to predict the intravascular volume status as well as pulmonary congestion and pulmonary volume status in hemodynamically unstable patients [39].

Several studies have compared the physical examination findings to POCUS findings to understand and improve the diagnostic accuracy of these findings. In a study by Saha et al. in the outpatient cardiology clinic, 51% patients were noted to be euvolemic by IVC assessment and clinical examination while the discordance between IVC assessment by POCUS and JVP assessment by physical examination was 32%, with POCUS proving more accurate [87]. In another study in the outpatient hemodialysis unit, 39% of patients who presented at or above dry weight were hypovolemic while 10% of the patients who left HD at or below goal weight were still hypervolemic by IVC assessment [88].

Table 1. Sensitivity/specificity in assessment of intravascular volume (volume overload)

Method of volume assessment	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Diagnostic accuracy
Tachycardia [4]	17%	94%			
Orthostatic hypotension [9]	29%	81%			
Dry oral mucosa [4]	49%	87.8%			
Jugular Venous Pressure >8 cm [12,13]	47-92%	93-96%			
Axillary sweat [4]	50%	82%		84%	
Abnormal skin turgor (sub clavicular) [4]	73.3%	79%			
Abnormal skin turgor (forearm) [4]	68.3%	67.8%			
Auscultation for crackles [22]	51% (43-60%)	79 % (73–84%)			
Crackles for severe congestion [55]	9%	98%	100%	78%	
Crackles and edema for severe congestion [55]	13%	97%	90%	33%	
Chest X-ray [91]	46%	80%	Not available	Not available	58%
CVP [32]	76%	62%			
IVC assessment (Respiratory variation) [48]	63%	73%	Not available	Not available	
Lung US [52]	88%	90%	Not available	Not available	
Carotid blood flow with Passive leg raise [39,84]	94%	86%			

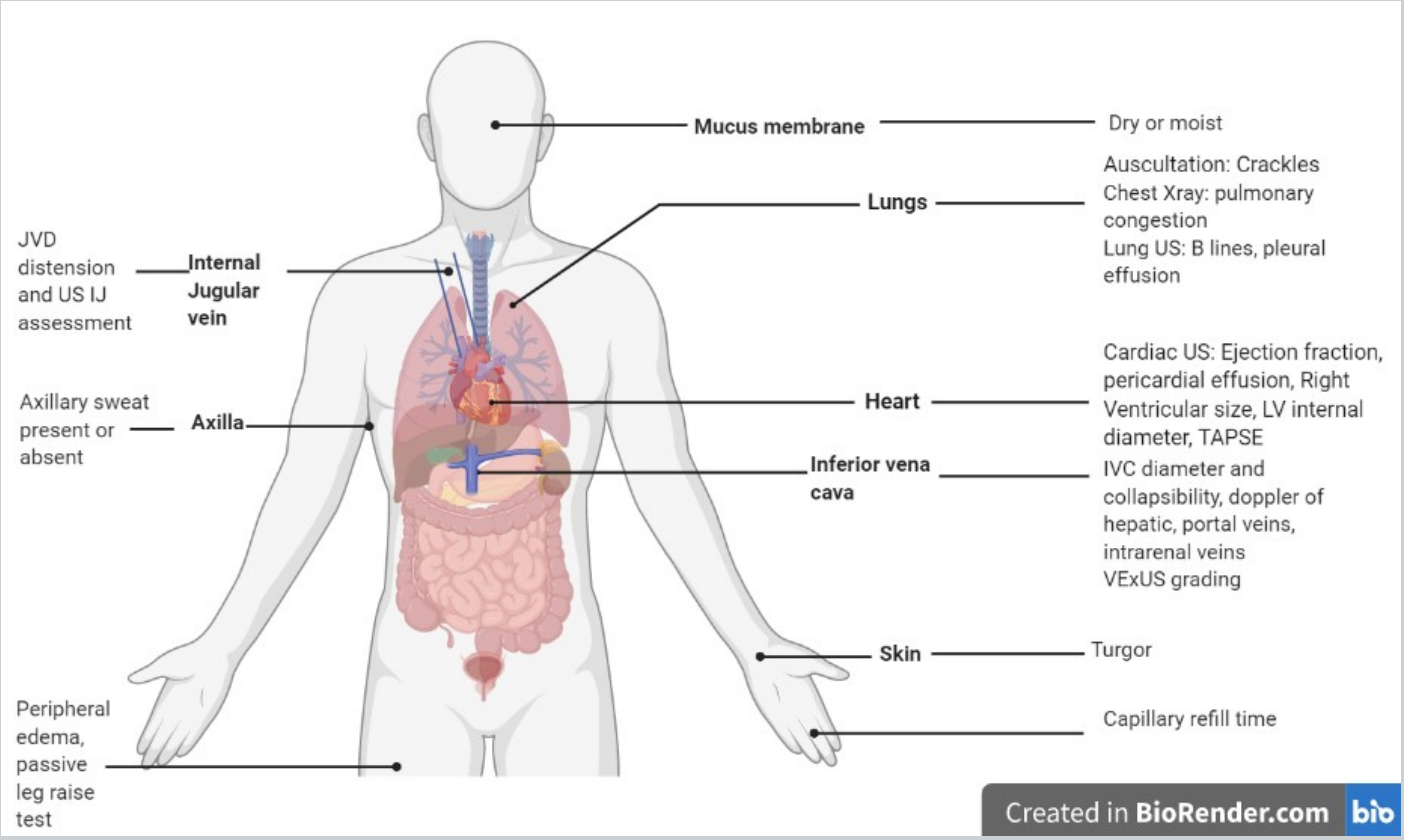

Figure 5. Schematic of Integrated Volume Assessment (Created with BioRender.com).

Similarly, the LUST study demonstrated that peripheral edema was absent in as many as 87% and 80% of assessments where lung US indicated moderate and severe lung congestion, respectively [55]. Peripheral edema had virtually no discriminatory power (moderate congestion: AUC 0.54; 95% CI, 0.50 - 0.58; P = 0.05 and severe congestion: AUC 0.56; 95% CI, 0.50 - 0.62; P = .03) [55]. The study also found a poor agreement between US B-lines and pulmonary crackles. Crackles had a limited discriminatory power for the diagnosis of mild, moderate, or severe lung congestion as assessed by US (mild lung congestion: AUC = 0.61; 95% CI, 0.57 to 0.64; P = 0.001; moderate congestion: AUC = 0.65; 95% CI, 0.61 to 0.70; P = 0.001; severe congestion: AUC 0.68; 95% CI, 0.62 - 0.74; P = 0.001) [55]. The combination of crackles and peripheral edema showed a satisfactory to low positive predictive value (ranging from 79% for mild congestion to 33% for severe congestion) and a high to moderate negative predictive power (ranging from 90% for severe congestion to 48% for mild congestion) [55].

With the limitations of the conventional methods compared to US techniques, US is used more frequently with better predictive capability and objective assessment of volume. However, misdiagnosis based on POCUS findings especially due to limitations of US and lack of experience can also lead to fatal errors in management [59]. Hence, it is imperative that we do not rely on one single tool, but rather integrate both pertinent physical examination and POCUS findings for better probability of coming to the right diagnosis. Several studies have suggested such integrative methods.

US IVC assessment of volume can be limited when used alone as described earlier. However, focusing management based solely on lung US can also sometimes result in intravascular volume depletion. Hence integrating both IVC and lung US has been proposed by Thomas et al. in more accurate estimation of dry weight in hemodialysis patients as IVC and lung US measure intravascular compartment and extravascular lung water respectively [89]. Lung and IVC US done immediately before and 30 minutes after the 4th session of hemodialysis based on clinically defined dry weight showed that the number of B-lines reduced from 12.7 ± 9.7 to 4.8 ± 6.6 (P < 0.001) and IVC collapsibility index increased from 0.23 ±0.09 to 0.53± 0.16 (P < 0.001). The coefficient of correlation between reduction in the number of B-lines after HD and change in the IVC collapsibility index was 0.33 (P = 0.004). Basal crackles were present in only 19% of patients with B-lines ≥4 but none of the patients with B-lines ≤4 had crackles [89].

Tri-POCUS approach in combining lung US, focused cardiac ultrasound, and venous Doppler ultrasound for accurate volume assessment was proposed by Koratala

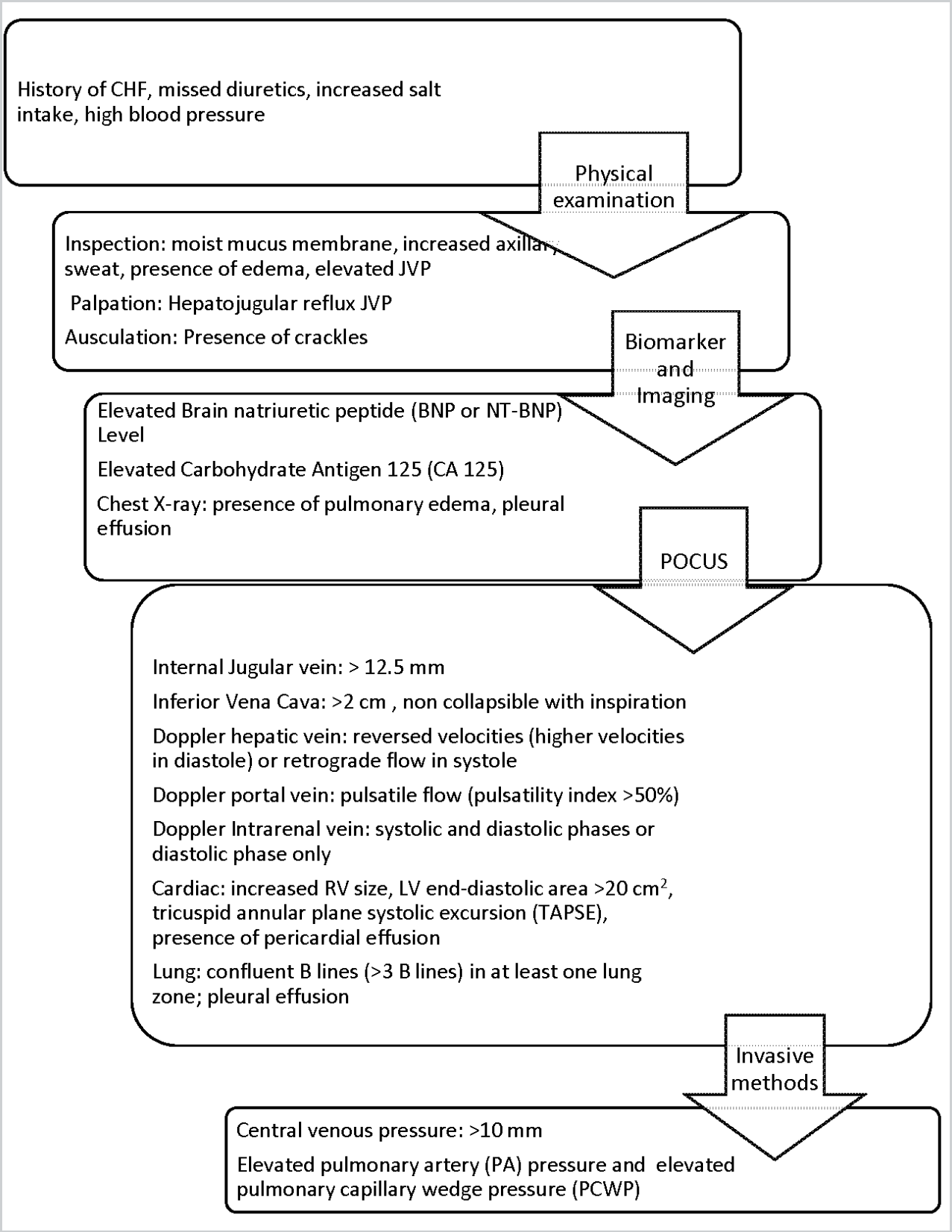
History of CHF, missed diuretics, increased salt intake, high blood pressure
Physical examination
Inspection: moist mucus membrane, increased axillary sweat, presence of edema, elevated JVP
Palpation: Hepatojugular reflux JVP
Ausculation: Presence of crackles
Biomarker and Imaging
Elevated Brain natriuretic peptide (BNP or NT-BNP) Level
Elevated Carbohydrate Antigen 125 (CA 125)
Chest X-ray: presence of pulmonary edema, pleural effusion
POCUS
Internal Jugular vein: > 12.5 mm
Inferior Vena Cava: >2 cm , non collapsible with inspiration
Doppler hepatic vein: reversed velocities (higher velocities in diastole) or retrograde flow in systole
Doppler portal vein: pulsatile flow (pulsatility index >50%)
Doppler Intrarenal vein: systolic and diastolic phases or diastolic phase only
Cardiac: increased RV size, LV end-diastolic area >20 cm^2, tricuspid annular plane systolic excursion (TAPSE), presence of pericardial effusion
Lung: confluent B lines (>3 B lines) in at least one lung zone; pleural effusion
Invasive methods
Central venous pressure: >10 mm
Elevated pulmonary artery (PA) pressure and elevated pulmonary capillary wedge pressure (PCWP)

Figure 6. Algorithm for Systemic Approach to Volume Assessment: This is an algorithm that we propose will help with systematic approach to integrative volume assessment for diagnosing hypervolemia. Assigning a score system to each of the findings with higher scores to cardiac, lung and vascular ultrasound for volume assessment would be very useful tool to precisely diagnose volume status. Such tool needs to be studied and validated before widespread use. This approach will integrate POCUS to conventional methods and eliminate the shortcomings of individual methods.

et al. to overcome the limitation of individual methods [19]. Integrated cardiopulmonary ultrasound with assessment of cardiac contractility, IVC assessment, and lung US shortened the time to definitive diagnosis of pulmonary edema (17 ± 6 versus 104 ± 34 minutes, $P \leq 0.001$) in a study of 128 patients [90].

Another tool that uses integration of various US methods is the VEXUS scoring system described above which integrates the IVC, hepatic vein waveform and portal vein pulsatility, renal vein Doppler for better assessment of venous congestion and fluid overload. The integration of these 4 parameters would negate the pitfalls of the individual method. In a study of 30 patients, resolution of AKI injury showed significant correlation with improvement in the VEXUS grade (P = 0.003), with significant association between changes in the VEXUS grade and fluid balance (P = 0.006) and a significant difference in fluid balance between the VEXUS score improving group (0.20 ± 1.24 L /day) compared to the no change group (1.67 ± 1.03 L/day) and the worsening group (1.00 ± 0.00 L/day, P = 0.03) [81].

We propose a stepwise approach to the volume assessment starting with conventional physical examination as feasible followed by combination of various POCUS methods (Figure 5 and 6). We will have a very good diagnostic tool if we use a scoring system with all the available physical examination and POCUS findings to decide on volume status using an aggregate score. We suggest assigning more weight to POCUS findings because of their ability to predict the volume status better than physical examination findings. Integration of these conventional and POCUS findings in a systematic way and using scoring system would provide valuable information in volume status management much closer to precision than use of these individually. Future clinical score development and validation using all these conventional and POCUS variables would be necessary and useful clinical practice tool. This is only a proposed scoring tool and needs to be validated. Future studies are recommended to validate such tool if it were to be developed.

Limitations

All these methods are subject to examiner or operator's knowledge, skills and bias in addition to patient specific characteristics and hence caution should be used when interpreting these individually. If used by inexperienced operators, POCUS can provide inaccurate findings and lead to wrong diagnosis and error in management. Lack of proper training, appropriate credentialing process and ongoing quality assurance before widespread use can lead to failure to identify pitfalls in the techniques and cause patient harm. Currently we do not have external validation for POCUS findings nor validation with the clinical outcomes which can lead to incorrect diagnosis and prognostication.

Conclusion

POCUS has provided an important clinical tool to support our clinical examination and conventional methods in assessment of intravascular volume. None of the tools currently available provide perfect assessment without any pitfalls when used alone. However, with integration of all the pertinent clinical and POCUS tools using a scoring system, we can ensure precise volume assessment. With enforcement of validation methods, proper training, and formalized credentialing process, we can ensure its accuracy and reliability. In the meantime, recognizing the limitations, we should encourage wise integrated use of the various clinical and POCUS methods in our daily practice to provide precision care to our patients.

Disclosures

This manuscript is original and is not under consideration for publication elsewhere. The authors do not have any conflicts of interest or financial disclosure.

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FEB 2022 vol. 07 Kidney | POCUS J | 78

Machine Learning in Point of Care Ultrasound

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What are Machine learning and Deep Learning?

When a patient presents to the ED, clinicians often turn to medical imaging to better understand their condition. Traditionally, imaging is collected from the patient and interpreted by a radiologist remotely. However, scanning devices are increasingly equipped with analytical software that can provide quantitative assessments at the patient's bedside. These assessments often rely on machine learning algorithms as a means of interpreting medical images.

A machine learning (ML) algorithm is able to utilize presented data to adapt and learn without following explicit instructions. ML is a branch of artificial intelligence (AI) and has garnered a great deal of attention over the past decade, due in large part to substantial advancements in data processing and improvements in model performance. ML has proven to be a powerful method for interpreting complex data. Clinicians may understand all the information necessary to classify a patient's condition, but seldom can they derive an equation that communicates precisely what information is relevant and irrelevant. ML excels at this task and permits scientists to develop solutions without knowing how to explicitly code the answer. In the most common form of ML, called supervised learning, scientists provide data inputs (called features) and corresponding class labels. The machine learning algorithm then determines what input features are relevant to predict the class labels, thus generating a model that can take in novel features and provide a predicted class label as output.

One of the most successful methods for solving medical imaging problems is a subfield of machine learning called deep learning (DL). Deep learning was inspired by the complex neural architecture of the human brain, which is organized into interconnected layers of neurons and can solve incredibly complex problems. In the primate visual cortex, simple photoreceptor input is passed through convolutional layers in the ventral visual stream of the brain. Each successive layer produces increasingly complex representations of the photoreceptor input, which permits humans to classify the objects and interpret the scenes they see. Similarly, deep learning algorithms simulate the ventral visual stream by passing image information through multiple layers of a convolutional neural network (CNN). These networks process simple pixel information, form new complex representations, and pass those representations on to subsequent layers for eventual image classification [1].

To train a CNN to classify images, pixel values are passed into the initial layer of neurons which are activated by the information (Figure 1). The activations are then fed forward into additional hidden layers which further process the data. The features generated by this process are fed through a final activation function, which provides a classification label in the output layer. To improve model accuracy, algorithm predictions are compared to provided labels. A cost function assesses the difference between model predictions and actual values, awarding a proportional penalty to the model. The goal of the training process is to minimize the cost or penalty awarded to the model. Using an optimization technique called gradient descent, the response weight of each individual neuron in the network is iteratively tuned such that the final classifications better match the expected output, thus reducing the penalty assessed by the cost function. After training on a corpus of images, a novel image can be fed into the algorithm and a predicted classification will be output.

Over the past several years there have been huge advances in the use of ML and DL algorithms to address a number of challenges clinically. DL algorithms have been extensively used within the field of radiology where they are used to perform numerous tasks, including segmentation of anatomical structures or local lesions, detection of probable tumors, and classification of lung and breast nodules [2,3]. A prominent example of how DL is rapidly changing the field of radiology can be seen in chest X-ray advancements. In 2017, with the release of the world's largest publicly available chest X-ray dataset (over 100,000 frontal-view X-ray images) by Stanford and the NIH [4], P. Rajpurkar et al. developed a DL system called CheXNet that could automatically detect and classify 14 different diseases on chest X-ray [5,6]. While there are some concerns surrounding the validity of human to algorithm comparisons [7], their system was able to achieve a comparable detection rate to expert radiologists for most diseases and demonstrated the promise of DL systems within medical imaging [8].

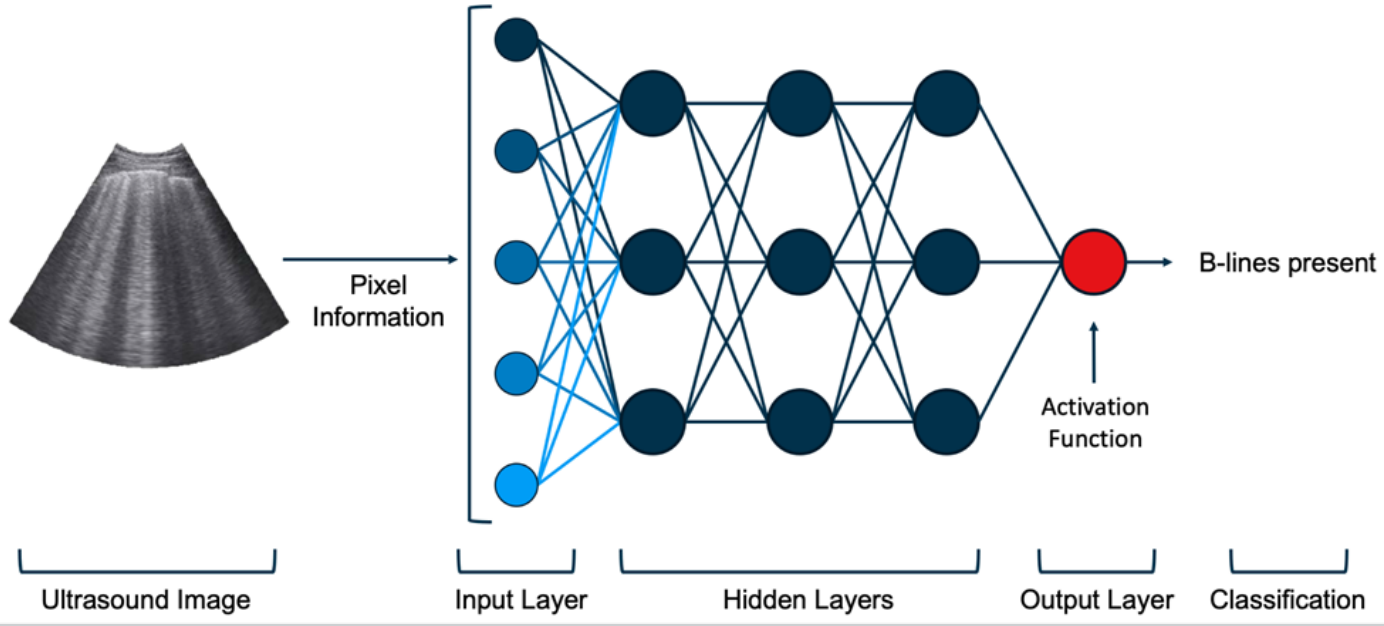

Figure 1. Example convolutional neural network for ultrasound. Here we present a simplified network architecture for a model designed to detect the presence or absence of B-lines in a lung ultrasound image. The model takes in raw data, in this case pixels from the lung ultrasound image. Neurons in the input layer, represented here by circles, are activated to varying degrees by the pixels. These activations are passed forward through several convolutions in the hidden layers. Final activation values are fed into the activation function in the output layer. The output is a binary classification: either presence or absence of B-lines.

Challenges to greater adoption of DL in POCUS

The example above demonstrates the potential of ML systems to improve clinical care for patients as well as assist radiologists with their clinical workload. However, despite rapid advancements in many medical imaging modalities, similar applications of ML algorithms to point of care ultrasound (POCUS) have been slower to arrive. This discrepancy is present for a number of reasons. First, unlike POCUS imaging modalities such as chest X-ray, CT, and MRI, have standardized imaging protocols. Hospital image archiving infrastructure was designed to store and save imaging data for later use. As a result of the persistent imaging infrastructure for these modalities large, organized imaging datasets have been developed that can be more readily interrogated by DL algorithms.

In contrast, images and video acquired at the bedside using POCUS are often used for immediate physician support and not always permanently archived for later analysis. Additionally, the point of care setting inherently introduces variability in data quality even when collected by the same sonographer. Variation in sonographer skill level, image acquisition order, and technique further complicates ultrasound datasets. Even in well-performed scans, imaging distortion and artifacts are often an inescapable reality for POCUS. This results in ultrasound images containing a great deal of “noise” or randomness in the data. Variability is further compounded when combining images from different scanner manufacturers or academic centers into a single dataset. Additionally, ultrasound images often lack global reference structures, making it difficult to determine exactly where on a patient’s body an image was collected. Finally, as an imaging modality, POCUS is relatively new compared to chest X-ray, CT, and MRI, only achieving widespread use in hospitals in the 1990s [9]. Taken together, these reasons explain why there are relatively few DL applications for POCUS compared to other imaging modalities.

Nonetheless, the last few years have seen an explosion of novel DL applications within POCUS. DL is uniquely suited for analysis of POCUS because it is able to generate high-level abstractions from a wide array of raw imaging data of varying quality. This ability to “cut through the noise” and draw abstractions and note otherwise missed patterns has been one factor leading to greater use of DL within POCUS. Increased interest in DL has come in part due to unique computational approaches to address the obstacles previously mentioned. Both traditional machine learning techniques (i.e. random Forest classifiers, support vector machines) and deep learning methods (i.e recurrent neural networks (RNN), auto-encoders), have been employed on ultrasound datasets with good success. Additionally, researchers have utilized innovative techniques such as transfer

learning to circumvent some issues related to limited and inconsistent datasets. Transfer learning is the process of initializing a DL model with weights derived from another training task and fine-tuning the model to perform a new task with the goal of reducing the number of trials necessary to learn a similar task [10,11]. For instance, a model trained to accurately identify and segment straight lines may be retrained on a carotid ultrasound dataset in order to identify and segment the arterial wall. This approach has the benefit of generally requiring fewer class labels in the training set in order to develop a successful algorithm.

DL algorithms have the potential to further increase the utility and adoption of POCUS. Many important uses of ML applied to POCUS are outside the scope of this review, but also include DL algorithms applied to enable novice sonographers in acquiring the best image [12] and as educational tools for medical students and residents providing procedural training on needle guidance for epidural anesthesia [13]. Herein we will discuss potential and emerging clinical uses of ML approaches applied to POCUS.

Current Clinical Applications of ML within Ultrasound

Here we will briefly highlight some of the clinical ML algorithms that have been developed for POCUS. To date, there are relatively few real-time ML algorithms available in POCUS (Table 1). With the exception of a few commercially available models, the majority of ML algorithms were developed for US applications using datasets captured from retrospective studies. One barrier to greater adoption of ML models within POCUS is the need to implement software in real-time on the ultrasound device hardware itself. Adoption of ML in POCUS is challenging not only because software and hardware must be integrated to enable real time applications, but also because most recently developed ML models lack sufficient clinical validation and FDA approval to be used in the clinical setting. While this regulatory milestone may seem distant, it has already been achieved for similar medical imaging applications. In 2018 the FDA approved a retinal imaging device with onboard artificial intelligence that could make diagnostic decisions, a first of its kind innovation [14]. As researchers continue to develop ML models for ultrasound, it is important to note that given adequate implementation, many of these models can be adapted for POCUS devices in the near future.

As mentioned before, the majority of new ML algorithms within US have been applied using DL architectures. Some of the most significant advances in DL applied to POCUS have taken place within echocardiography. Here, a number of models have been developed for a wide number of classification, segmentation, and detection tasks. A frequently used DL application involving both segmentation and biometric measurements has been the rapid determination of cardiac ejection fraction (EF). In order to accurately determine EF using echocardiography, determination of cardiac cycles–namely, end-diastole and end-systole–is necessary. Some groups such as Dezaki et al. have successfully used ML models to accurately determine cardiac cycles [15] and a number of other groups have also successfully trained DL models to segment various chambers of the heart using recurrent neural networks (RNN) and CNNs [16–18]. Furthermore, the automation of EF and cardiac volumes using ML has been shown to have excellent agreement between automated and manual approaches, with increased efficiency and reproducibility of measurements [19,20].

There has also been significant interest in applying ML algorithms to lung ultrasound. Lung ultrasound has gained increased use in the POC setting due to the wide number of clinically useful assessments it provides [21]. The quantitative assessment of B-line score (BLS) has become an important tool for assessing pulmonary congestion using POCUS [22]. B-lines are hyperechoic reverberation artifacts arising from the pleural surface that extend to the bottom of the screen without fading and move in tandem with lung sliding. Total BLS can be used to determine fluid overload (FO) severity score and a number of studies have demonstrated that BLS accurately quantifies pulmonary congestion outperforming the physical exam and chest x-ray [23–25]. Additionally, in the point of care setting, rapid assessment of a patient's volume status can be a crucial tool in guiding clinical interventions. Yet, widespread use of this technique is limited partly due to the tedious nature of the assessment.

A number of groups, including our own, have developed DL models using CNN to automatically quantify B-line scores from POC lung ultrasound video clips. Recently, B. Christiana et al. developed a supervised CNN trained on 400 lung ultrasound clips to calculate total BLS in emergency department patients. They achieved a binary classification (B-lines present versus absent) sensitivity and specificity of 93% and 96% compared to an expert interpreter. In multiclass classification of B-line severity their DL model achieved a linear weighted kappa of 0.65 vs an interrater reliability of 0.87 [26]. Our own group has developed a DL model that uses a transformer block architecture CNN trained on 91 hemodialysis patients with ESRD to calculate total BLS and severity level. In preliminary results, our DL model demonstrated a binary classification (presence versus absence of B-lines) accuracy of 87.3% and a total BLS classification (scored 0-4) accuracy of 60.5% [27].

Point of care lung ultrasound has also shown great

Table 1. Discussed studies on the application of machine learning in ultrasound. Due to differences in study design, inter-study performance cannot be compared. Refer to original studies for details of study design. Acronyms: ED - end diastolic; ES - end systolic; RNN - recurrent neural network; LSTM - long short-term memory network; CNN - convolutional neural network; DSC - Dice score coefficient; EF - ejection fraction; LV - left ventricle; FASP - fetal abdominal standard plane; FFASP - fetal face axial standard plane; FFVSP - fetal four-chamber view standard plane; CKD - chronic kidney disease; DVT - deep venous thrombosis; ICC - interclass correlation coefficient; CI - confidence interval. (con't next page…)

Authors	Application	Model	Performance
Dezaki et al.	Cadiac: cycle phase determination (ED vs ES)	Residual RNNs (ResNet + LSTM)	R^2 score = 0.66 Error ED = 3.7 Error ES = 4.1
Smistad et al.	Cardiac: LV segmentation	CNN (U-Net [64])	DSC = 0.86 ± 0.06
S. Chen et al.	Cardiac: plane detection, LV detection, LV segmentation	PSPNet + temporal affine network (TAN)	DSC = 0.91
Knackstedt et al.	Cardiac: EF	AutoLV	ICC = 0.70-0.83
Thavendiranathan et al.	Cardiac: LV volume & EF	Probabilistic contouring algorithm composed of a Bayesian framework, hierarchical K-means clustering, and probabilistic boosting tree.	Correlation with cardiac magnetic resonance measurements: ED volume = 0.90 ES volume = 0.96 EF = 0.98
F. Dominika et al.	Cardiac: EF	LVivo EF (DiA Imaging Analysis)	Performance relative to calculated EF via 3D echocardiography: Pearson correlation = 0.92 (95% CI 0.87-0.95) Mean difference = 0.61% (95% CI -0.68-1.89%)
Nafee et al.	Extremities: DVT	Ensemble classifier	Concordance statistic = 0.69
Tanno et al.	Extremities: DVT	CNN	F1 score = 90%
H. Chen et al.	Fetal: plane detection (FASP, FFASP, FFVSP)	Transferred RNN (T-RNN): CNN + LSTM	Accuracy: FASP = 0.91 FFASP = 0.87 FFVSP = 0.87
Jang et al.	Fetal: abdominal circumference	CNN + U-Net	Accuracy = 87.1%
Gao et al.	Fetal: anatomy classification	T-CNN	Accuracy = 91.5%
Ravishankar et al.	Kidney: segmentation	Ensemble classifier with gradient boosting	DSC = 0.83
Wu et al.	Kidney: segmentation	Cascaded DenseNet	Mean intersection over union = 0.83
C. Chen et al.	Kidney: CKD detection	Support vector machines	5 stages: Accuracy = 70%
Kuo et al.	Kidney: CKD detection	ResNet	5 stages: Accuracy = 85.6%

Table 1 (con't…). Discussed studies on the application of machine learning in ultrasound. Due to differences in study design, inter-study performance cannot be compared. Refer to original studies for details of study design. Acronyms: ED - end diastolic; ES - end systolic; RNN - recurrent neural network; LSTM - long short-term memory network; CNN - convolutional neural network; DSC - Dice score coefficient; EF - ejection fraction; LV - left ventricle; FASP - fetal abdominal standard plane; FFASP - fetal face axial standard plane; FFVSP - fetal four-chamber view standard plane; CKD - chronic kidney disease; DVT - deep venous thrombosis; ICC - interclass correlation coefficient; CI - confidence interval.

Authors	Application	Model	Performance
Christiana et al.	Lung: B-line score	Custom shallow CNN (10 layers)	Presence vs absence: Sensitivity = 93% Specificity = 96% Severity (0-4): Kappa = 0.65
Sonko et al.	Lung: B-line score	Autoencoder + CNN	Presence vs absence: Accuracy = 87.3% Score (0-4): Accuracy = 60.5%
Correa et al.	Lung: pneumonia	Custom feedforward neural network (3 layers)	Sensitivity = 91% Specificity = 100%
Born et al.	Lung: COVID detection	CNN (VGG-16)	Sensitivity = 0.96 Specificity = 0.79
J. Short et al.	Lung: auto mated B-line counting	Auto B-lines (GE Healthcare Venue Go)	Correlation with expert interpretation: ICC = 0.794 (95% CI 0.736-0.840)

promise in the accurate diagnosing of community acquired pneumonia (CAP). It has demonstrated excellent diagnostic capabilities when performed by a trained sonographer compared to both clinical assessment and chest X-ray, while also avoiding unnecessary radiation exposure in vulnerable patients such as pediatric populations [28–30]. However, lung ultrasound is not included in the diagnostic workup for CAP partly because of inter-operator variability of lung ultrasound and training. DL approaches aimed at reducing these barriers are another emerging trend. In 2018, Correa et al. developed a neural network trained on 1450 CAP-positive ultrasound frames from a hospitalized pediatric population in Peru. The algorithm was successful in correctly identifying pneumonia infiltrates with 90.9% sensitivity and 100% specificity [31].

More recently, amidst the 2020 COVID-19 pandemic, there has been increased attention paid to increasing the diagnostic ability of clinicians to detect the presence of the novel coronavirus in patients. To this end, Born et al. developed a deep CNN trained on over 1100 COVID-19 confirmed lung ultrasound images to achieve a detection sensitivity of 0.96 and specificity of 0.79 and F1-score of 0.92 in a 5-fold cross validation [32]. The authors provide an open-access web service (POCOVIDScreen) that deploys the predictive model, allowing clinicians to both perform predictions on ultrasound lung images and upload their captured images to add to the database.

Use of POCUS within nephrology has also increased in use over the past several years. In patients with chronic kidney disease (CKD), volume overload plays an important role in the disease pathology by complicating cardiovascular pathophysiology leading to increased cardiovascular morbidity and overall mortality [33,34]. For patients with end-stage renal disease (ESRD) on hemodialysis, it has also been shown that the extent of volume overload correlates with adverse cardiovascular events [35]. Therefore, for the nephrologist, close monitoring of their patient's overall volume status is important in the clinical management of patients. Thus, POC lung ultrasound (and BLS quantification) has also become an important tool in the nephrologist's arsenal. However, other ML advancements within renal ultrasound include the accurate segmentation of the kidneys, yielding rapid and accurate measurement of renal dimensions in patients by groups such as Ravishankar et al. and Wu et al. [36,37], as well as the detection of various stages of CKD by groups such as Chen et al. and

Kuo et al. [38,39].

Fetal measurement is another widely used application in POCUS. In the emergency room, rapid and accurate assessment of fetal parameters such as crown-rump length and classification of the abdominal standard plane, are important to avoid misdiagnosis and guide appropriate interventions [40]. Several groups have developed deep learning models for fetal exams. In a two -step process, Jang et al. first developed a CNN to identify the abdominal standard plane and then trained a model to segment and estimate fetal abdominal circumference from fetal ultrasound images [41,42]. Gao et al. developed a CNN that categorized abdominal freehand sweep images into four categories: fetal abdomen, heart, skull, or other. They trained two models, one using only obstetric ultrasound images and a second that employed transfer learning, using a pretrained ImageNet model and fine-tuning it on obstetric ultrasound images. Transfer learning improved classification accuracy in all categories of fetal anatomical structures compared to their non-transfer learning approach [43].

The final clinical application of ML for POCUS discussed here is deep-venous thrombosis (DVT) screening. POCUS is an important tool for physicians treating potential DVT patients within the emergency room as well as in the inpatient setting. POCUS can guide clinical decision-making for patients at risk for, or suspected of having, a pulmonary embolism [44]. During the exam, the deep veins of the lower extremity are compressed along their course and areas of low compressibility suggest potential thrombus formation at that location. Recently, Nafee et al. sought to evaluate the performance of two ML models they developed versus a validated DVT scoring system in acutely ill patients. Their study demonstrated that both of their ML apporaches outperformed the validated manual scoring system in predicting venous thromboembolism (VTE) (c-statistic: ML methods = 0.69 and 0.68, manual scoring system = 0.59) [45].

Other models such as that by Tanno et al. have aimed to increase classification accuracy of DVT scans by automatically detecting the extent of vein compressibility in DVT scans [46]. Researchers proposed a dual-task CNN to predict vein compressibility with an F1 score of 90% when evaluated on 1150 5–10 s compression image sequences from 115 healthy volunteers resulting in a data set size of approximately 200k labelled images. As further development continues, these advancements may greatly increase the accessibility and clinical usage of this already impactful diagnostic study.

Commercially Available products utilizing ML

Of note, companies such as Mindray and GE have utilized ML and DL based algorithms in commercially available echocardiography products to perform automated tasks such as automated EF calculation, LV border identification, and chamber length calculations (Mindray North America, Mahwah NJ; GE Healthcare, Chicago IL). Newer devices entering the market are now often branded with “AI enabled” capabilities, such as left ventricular outflow tract (LVOT) plane identification and Doppler placement (see: GE Venue and Mindray). These tools are beginning to make their way into newer POCUS devices as well. Companies like Butterfly Network, Bay Labs, and Clarius have released POCUS probes that contain AI-enabled cardiac algorithms for automated EF estimation as well as cardiac chamber segmentation (i.e. Butterfly Network’s IQ probe).

There is also commercial interest and new adoption of automated B-line counting algorithms within POCUS. Notably, GE has incorporated an auto B-line counter within their new suite of GE Venue Go POCUS devices. Their model uses computer vision and DL approaches, including a proprietary CNN, to automatically detect and count B-lines in lung ultrasound scans. A study by J. Short et al. found that automatic counting of lung B-lines was consistent with visual counting, as performed by experts in the field and both systems showed a high intra- and interobserver reliability [47]. Other device manufacturers such as Mindray have similarly developed their own automatic B-line counting algorithms using a mixture of traditional computer vision systems and DL approaches.

Interestingly, the clinical ML software market has grown to now support firms whose business models almost entirely center around developing novel algorithms for clinical use intended for device manufacturers. DiA Imaging Analysis Ltd. is one notable firm in this category. They partner with ultrasound device manufacturers and large academic medical centers to develop AI-enabled solutions for ultrasound. Currently, as mentioned previously, much of the development for these solutions has focused on POC echocardiography, but additional interest has been shown in the development of AI-enabled abdominal algorithms as well. The company has additionally partnered with GE to offer the first AI-based solution for automated EF analysis on handheld ultrasound through the “LVivo EF” on GE’s Vscan Extend, which has been shown to yield similar EF values as 3D echocardiography [48]. As interest in DL applications within POCUS continues to blossom, it is likely that additional firms similar to DiA will emerge, outsourcing much of the ML innovation once developed in-house by ultrasound device manufacturers to specialized image analysis companies.

Future Steps & Upcoming Advancements

The dynamic and real-time nature of POCUS provides a major advantage over other imaging modalities such as CT and MRI. Yet, this also represents a major challenge for researchers developing ML algorithms for POCUS. A trained sonographer will rarely examine a single image frame to make a clinical assessment of a patient; rather, data from multiple frames are assessed simultaneously together to inform the clinician of a proper course of action. Within the broader context of deep learning, a known issue is that most state-of-the-art architectures are optimized for single image classification and that impressive performance does not necessarily generalize to video-type data, such as POCUS.

A variety of methods have been applied to try to generalize methods used for image classification to video classification. Perhaps the most direct implementation of this has been the use of 3D CNNs (as opposed to the 2D ones used for single image classification). For example, Hara et al. extended the state-of-the-art ResNet architecture to 3D by adjusting the original 3x3 kernels to 3x3x3 [49]. However, introducing 3D convolutions leads to significantly increased computational overhead and increases network complexity, hence yielding longer training times and increased likelihood of overfitting models [50]. Progress on this front has been made by mixing 2D and 3D convolutions and using *R(2+1)D* convolutions (wherein 3D convolutions are factorized into spatial and temporal convolutions) [51,52]. Such architectures show great promise for application in POCUS, but the complexity of such networks leads to requirements for large amounts of data, which are often unavailable.

Another approach, first proposed by Simonyan et al., involves processing video data as two separate streams: a spatial and temporal stream [53]. The spatial stream is designed to classify still video frames and typically consists of a 3D CNN or a conventional 2D CNN which sequentially processes frames. The temporal stream is meant to capture inter-frame changes and is created by combining optical flow data from several frames. Generally, these two-stream CNNs outperform both conventional 2D and 3D CNNs for video classification. Howard et al. applied such a two-stream CNN to automatically determine the scan view from echocardiography data. Such two-stream CNNs can potentially lower the computational overhead for POCUS analysis and classification [54].

A major area of interest in our group and others has been the application of attention-gated networks to DL ultrasound. Attention mechanisms attempt to better mimic human perception by using surrounding local information in the data to contextualize a specific target. Attention models have been heavily used for natural language processing (NLP) tasks, where integrating information from potentially distant parts of a sentence is necessary to accurately translate a given word [55]. Here, transformer block architectures have been used with success [56]. Attention mechanisms were first used by Mnih et al. in a recurrent neural network (RNN) for image classification [57], but has since been applied to a variety of ultrasound image analysis including in fetal ultrasound scan plane detection [58]. Attention models could prove useful in a variety of POCUS models including B-line score (BLS) determination from lung ultrasound. Accurate determination of BLS often depends on assessing adjacent frames rather than relying on a single frame. Attention models have the additional advantage of giving insight into which video time frames and what image content the algorithm is attending to for deriving its classification, thereby potentially improving interpretability.

Additionally, researchers have developed alternative approaches to identifying optimal network architectures through neural architecture search. Generally, network architectures are designed by data scientists using some *a priori* hypothesis of underlying data structure. This time-consuming task leaves the entirety of alternative network architectures largely unexplored. To address this issue, scientists and Google's AI division developed a neural architecture search, where machine learning techniques are used to optimize the network architecture while training the network itself [59,60]. This approach has been successful for improving the architecture of conventional (image-classification) CNNs and is now being applied to video CNNs. Piergiovanni et al. designed EvaNet, wherein they used an evolutionary algorithm to explore different layer types and combinations that could optimally represent the relationships between spatial and temporal aspects of videos [61]. Ryoo et al. designed AssembleNet, a network composed of multiple sub-network blocks that interprets input videos as multiple input streams sampled at different levels of temporal resolution [62]. AssembleNet is able to optimize the connectivity between both the sub-network blocks as well as the connectivity between the multiple variable-resolution streams. Such techniques are already being applied for medical image analysis. For example, Yan et al. developed MS-NAS (Multi-Scale Neural Architecture Search for Medical Image Segmentation) and applied it to outperform several state-of-the-art algorithms used for segmentation of CT images [63]. Given the temporal dynamics and acquisition complexities of ultrasound data, *a priori* hypotheses are unlikely to arrive at efficient network structures. Neural architecture search techniques, such as MS-NAS, will permit data-driven approaches to developing optimized algorithms that can address the broad range of ultrasound image processing

problems faced by clinicians.

Conclusion

In conclusion, we have introduced the concepts of machine learning and deep learning, reviewed current applications of these powerful tools in POCUS, discussed available commercial products utilizing machine learning, and explored promising future directions for machine learning on POCUS research. The utility of POCUS is largely derived from its capability for real-time inference and portability. While these factors present initial hurdles to the early adoption of machine learning in POCUS, they may also serve as the modalities greatest assets. Machine learning demands increasingly large datasets, sometimes needing millions of training images. POCUS is uniquely positioned to provide large datasets of video frames that could potentially be used for real-time algorithm training. Additionally, the portability of POCUS has the potential to provide a platform for rolling out machine learning applications in medical imaging to the entire world.

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Nuts and Bolts of a POCUN Program

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NUTS and BOLTS of a POCUN Program

For those that have experienced how much point of care ultrasound can positively impact patient care, the potential of an organized point of care ultrasound program is moderated by the reality of building such a program from scratch. We have watched novice and intermediate users ride the roller coaster of ambition and reality checks at each of the hands-on skills sessions across the nation. The first climb occurs on the morning of Day 1. Anticipation grows over how hard it might be to learn this skill, then peaks and dips into the exhilaration of seeing success with what feels like minimal guidance. A comprehension of attainability takes over, and after each hands-on session, confidence climbs fast. Day 2 begins with the courage of some experience, and the anticipation of more success. The questions start as the climb up the second hill begins: “This is practice changing! How do I start a program at my home institution?” The ride turns into a steady flow of dips, spins, and twists as facilitators use less guidance and allow for more struggle. The questions turn to statements as learners develop a metered sense of capability: “I NEED a program at my home institution. My colleagues are going to want to know how to do this too, and I want to develop my skills.”

The momentum is strong for physicians to integrate Point of Care Ultrasonography (POCUS) across the spectrum of ambulatory and inpatient care. Nephrologists can interpret and evaluate patients using point of care ultrasound in nephrology (POCUN) and it is becoming a key part of training [1]. The promise of POCUS for improved patient care is supported steadily as studies demonstrate how it can expedite more accurate diagnoses and improve outcomes [2,3]. Indeed, POCUN may be a key component of restoring interest in nephrology with ultrasound interpretation the second most desired topic for additional instruction [4]. So how does one get from attending a professional conference to something organizationally developed enough to be called a program in order to realize these benefits? Here are some basic questions to ask yourself (or your team!) to mature a POCUS learning experience into a structurally sound program.

BUILDING

Who Are Your Patients?

Making the biggest possible impact with POCUS requires an alignment of the POCUS user’s skillset with the patient’s needs. Patients with kidney disease use acute care services disproportionately and POCUS can decrease the burden of care experienced by a patient at a reduced cost to the system as a whole [5]. As a sub-specialist, a program’s scope can be narrowed and thus the impact concentrated. Asking “Who are your patients?” is really saying: “Define your core POCUS applications.” POCUS puts the power of ultrasound into the hands of the clinician already at the bedside [6]. Bedside physicians are hungry to learn techniques that improve their ability to diagnose patients—especially toward the elusive accurate volume assessment [7]. In the hands of a nephrologist, the addition of lung ultrasound alone to the POCUN toolkit can assist in assessments of lung water which can improve intradialytic ambulatory blood pressure control and changes in pulmonary edema in response to dialysis [8-10]. To complement lung POCUS, diagnostic assessment of the IVC, kidneys and bladder, and focused echo are limited POCUS exam additions that support a more accurate volume assessment. Ultrasonographic findings in COVID-19 may complicate the interpretation of lung ultrasound for volume assessments in particular [11]. Even as it appears the COVID-19 pandemic is waning, the experience exemplifies how emerging diseases can impact our diagnostic tools’ limitations.

Visualization of common kidney and bladder pathologies such as hydronephrosis, cysts, stones, prostatomegaly, and masses are possible with a basic POCUN skill set. Basic echocardiography can evaluate for pericardial effusion, gross valvular abnormalities, and gross assessments of ejection fraction. Assessment for maturation of the arteriovenous fistula and guidance of vascular access cannulation are also potential adjuncts to key procedural ultrasound skills for central venous catheter placement and renal biopsy [12,13].

Who is Your Team?

Knowing who to recruit will help expedite organization and communication at the early stages of program

design and eliminate obstacles during implementation and execution phases. The cornerstone of a program, of course, is the faculty that can use POCUS clinically and become part of the fabric of the program. Beyond capable physician faculty within the nephrology division that will perform the scans, relationships with others outside nephrology are critical to program success. Non-physician sonographers are part of those teams for many institutions, for example, and can be an outstanding asset for one-on-one hands-on instruction of learners. Having an established relationship with radiologists can lead to a robust image review and quality assurance team. Cardiologists are an excellent addition for focused echocardiographic reviews. Emergency medicine physicians benefit from decades of experience with POCUS implementation and education. Departmental collaboration increases the educator pool for all departments. Collaboration can also streamline impact on patient care. For example, a multi-department collaborative can perform as a committee when implementing standardized documentation of POCUS findings which would allow tracking of findings over time for an individual patient. Information Technology (IT) is crucial in developing an efficient and seamless way to store images for both review and billing purposes, not to mention integration into security frameworks so that personal health information (PHI) remains protected. Many of the newer handheld devices utilize wireless information uploading and cloud-based image storage. Successful image storage integration into existing structures such as picture archive communication system (PACS) is crucial. The biomedical and engineering teams also have a stake in equipment to be purchased by a hospital and used by faculty in the care of patients, especially at the inevitable point of needing repair or replacement. The support of your executive leadership can make for more fluid program-building as the development of a program from scratch inevitably requires investment for equipment and IT workflow solutions, even if the plan is simply to integrate into an existing electronic medical record and Digital Imaging and Communications in Medicine (DICOM) PACS storage solution.

Best Tools for the Job

If you are talking about clinical POCUS, then the choice is really between a handheld device and a small cart-based ultrasound. There are now multiple options in both categories making the devices competitive in class. **Table 1** provides a quick rundown of pros and cons for each. One place where they differ greatly is in price comparisons. Handhelds are increasingly subscription and cloud based. This means a pay structure with either yearly or monthly fees in addition to hardware costs in order to maintain access to image storing clouds and/or device tools for interpretation and education. In contrast, cart or laptop-based systems are currently still offered as one-time hardware costs with a more traditional warranty structure. The outright cost for handhelds ranges from $2000 to $8000 with subscriptions costing an additional amount yearly depending on subscription type (personal versus group license) [14,15]. Cart and laptop systems typically used in bedside applications range from $25,000 to $60,000 [16]. Program goals may change over time and with expansion so device demand can be expected to evolve. A new program for a nephrology practice with fellows may choose handhelds for inpatient and outpatient flexibility of using a mobile platform. An outpatient practice may choose to invest in a cart-based machine for a device that can provide excellent visualization for both procedural and non-procedural POCUS applications. One key feature setting apart larger and more expensive systems is pulsed-wave Doppler. Pulsed-wave Doppler is not required to perform core applications including lung, kidney, and bladder ultrasound, but can add information to advanced cardiac and renal vascular techniques.

Communication Planning

Patients can have a more positive healthcare experience and a better understanding of their diagnoses and care when POCUS is utilized [17,18]. A program administration communication strategy is key, but the most critical communication plan is at the patient level. How will you set expectations regarding the experience of an ultrasound and describe using patient-centered language what the grayscale means? Improved bedside doctoring is one of the most attractive parts of POCUS and effectively engaging the patient takes a different effort compared to the current workflow, i.e. sending the patient to a different department and communicating findings via the phone or the electronic medical record [19]. Having a high standard of communication helps achieve the value of bedside ultrasound. How will your team communicate abnormal findings in real time? How will your team communicate uncertainty and the potential need for additional or repeat testing based on your bedside findings? What implications do your bedside findings have? For instance, if in the outpatient visit you diagnose new large pleural effusions what is the pathway for care? What if you note a new kidney mass when you performed a study looking for hydronephrosis? Communicating abnormal or unexpected findings are already a part of every physician's toolkit; however, a plan for this type of POCUN communication should be considered a fundamental part of a program build. This is especially important with the advent of legislation similar to Pennsylvania Act 112 mandating written

Table 1. Quick Pros and Cons of Handheld and Cart or Laptop POCUS Devices

Handheld Pros	Handheld Cons	Cart/Laptop Pros	Cart/Laptop Cons
Handheld / pocket sized	Potential for displacement/ loss/ difficult to track	Better image quality due to better transducer quality	Less portable / maneuverable across multiple units
Can limit transducer style (and cost) based on focused applications	Limited applications if only one type of transducer purchased	Larger screen and controlling buttons	Dexterity at bedside also potentially limited due to size
Most with easy connections to cell phone / app-based	May require additional screen / tablet negating benefits of portability	Potential for all transducers needed on hand	More expensive than handheld devices

communication of "significant abnormalities" detected on imaging [20].

Quality Assurance and Image Review

Quality assurance (QA) and image review are a fundamental part of any POCUS program fulfilling many key functions including creating a teaching file of pathologic images, providing feedback to learners, building a learner image portfolio for credentialing, and communicating missed or incidental findings to patients. Setting up your team to include POCUS clinicians from other divisions and departments can become valuable when organizing the approach to image review and QA. Image review requires a reliable, retrievable, and organized collection of images to be stored securely. How to accomplish this can be fairly individualized, but there is one aspect that is universal: person-power. No matter what, a person or a team will need to have the time allotted to perform basic image review for quality assurance. When thinking about the image storage location, some of the most common solutions are a HIPAA compliant cloud, DICOM PACS, or third-party HIPAA compliant server. Transferring the images from the device to the storage solution will involve the IT team. Once uploaded, the POCUS clinical team will need a method to determine how images are selected for review. For instance, should all trainee-generated images be pushed to the patient's chart or should poor quality images remain sequestered in the image archiving solution? The method for organizing QA solutions is individualized to suit the needs of the participating reviewers and the institutional demands.

Some percentage of total images should be reviewed to ensure image acquisition and interpretation meets departmental thresholds for accuracy. Who participates in image review, how often it occurs, and what percentage of images are reviewed are part of the program design. Some programs will choose to QA 100% of images, whereas more established programs may only review 5-10% [21]. Generally speaking, the more novice the user, the more images should be reviewed per term. Therefore, any program design should consider the number of novice users when allotting time for this effort. An academic nephrology fellowship program may choose to integrate a tiered approach to image review. For example, the POCUS faculty would oversee a review session where the fellow performs primary image review of images collected by the entire program with guidance. In this way the fellow develops the skill of reviewing with oversight.

Establishing criteria for what constitutes a clinically adequate image supports users in performing clinically adequate scans as well as a structure for critique and improvement. The minimum of "pass/fail" image review does little to support the user in neither improving nor troubleshooting. Providing written or verbal feedback better supports the user and ultimately the patient.

A robust system for QA lays the groundwork for continuous quality improvement (QI). QI in POCUS is the process of evaluating the system as a whole and systematically investigating and implementing specific measures for the furtherance of patient care and trainee education using bedside ultrasound.

Maintenance of Skills: Credentialing, Certification, and Privileging

Kim, Thiessen, and Strony break down the differences between these terms as specifically applied to POCUS [22]. The residency-trained POCUS provider takes a different pathway to achieve competency compared to a practicing physician adding to their skills through a practice-based pathway. Whether credentialing is best for your new program is fully dependent on the existing structures present to ensure all physicians are qualified to practice at the level at which they are employed. Proponents of a requirement for credentialing and privileging emphasize the diversity of training pathways and the lack of POCUS milestone requirements from neither the ACGME for non-emergency medicine trained physicians nor most residencies. Without longitudinal oversight and milestone achievement as is expected for other skills such as taking a history and performing a

physical exam with a stethoscope, the concern is that there could be excessive variability in competency, especially when requiring a physician to self-referee [23]. Alternatively, credentialing and privileging requirements could be prohibitive to pursuing training in POCUS, as it raises a barrier based on an assertion that physicians could not be expected to effectively self-referee for a non-invasive diagnostic skill. In fact, the very fact that it is non-invasive is often held up as analogous to the use of the stethoscope, a skill in which no physician is required to demonstrate ongoing competency beyond their training years and for which one is not required to request special privileges [24].

Whether or not a system requests credentialing as a pathway to obtaining privileges, or permission to use POCUS is a reflection of the unique medical structure at each practice site. Certification programs can serve as surrogate practice-based pathways when residency pathways or hospital-based pathways are unavailable, or even in addition to those pathways. While not required to demonstrate competency, certification in aspects of clinical ultrasound—as can be obtained through the American Society of Diagnostic and Interventional Nephrology—serve as a bolster for nephrology faculty specializing in POCUS, signaling to peers and institutions that they are committed and capable in the field [25]. Ultimately, how a new program grapples with this grey area can be expected to be informed by the ongoing national conversations on these topics. As an increasing number of residency and fellowship programs incorporate POCUS training and associated milestones into their curricula, more specialties will be able to consider POCUS a core competency, thus potentially obviating the need for special privileges [26].

PROGRAM GROWTH and MAINTENANCE

Role of the POCUN Director

The aforementioned foundational structure is well-served by having a designated leader with clearly delineated responsibilities [21,27]. Even if a program plans to launch with a team of leaders, the benefit of having a single point-of-contact for more efficient communication between team members and the larger POCUS network at a site cannot be overstated. Just for the structure outlined thus far there is a need for cross-disciplinary collaborations, general program oversight, and a person to spearhead organization of QA/QI.

At every branchpoint of growth there is a corresponding number of responsibilities. Growth and maintenance will not likely occur without a designated POCUN Director. As each part of a program expands, the administrative burden grows. Growth in education such as the addition of a fellowship and education at the student or resident level requires recruitment, marketing, and curricular design. Growth in number of clinical users adds to the number of studies for QA as well as the responsibilities for oversight. Growth in the number of devices corresponds to the number of times something needs a fix, repair, or simply guidance for use. The role and responsibilities of POCUN Director deserves protected time to be most effective.

Fellowship

How does a program become self-sustaining? Expanding the core nephrology faculty is an obvious first goal in order to allow for shared responsibilities across the spectrum of administrative and educational need. There is no one best way to expand the faculty leadership cohort. Integrating POCUS faculty development into existing responsibilities is possible with approaches curated to the specialty with respect to demands on the participants time and in tandem with learners at different career stages [27-29]. Efficiency in leadership tasks like image review and quality assurance programming can be expected to be dependent on supported time for a coordinating program director [30].

Integrating POCUS into the core fellowship curriculum is one way to grow a foundational program into a sustainable cohort of skilled bedside sonographers and expand a programs capacity for image review. Koratala, et al. describe one such method of building POCUS education and skill development into the first 18 months of nephrology fellowship training [31]. Offering a dedicated fellowship in POCUS is also an option for further expansion into educational POCUS training at every level of the medical career pathway which would be expected to translate into a more longitudinally trained cohort. As described by Koratala, et al., “As more medical students and residents are trained in POCUS, it is conceivable that the focus of POCUS training during fellowship will shift from ‘performing’ the examinations to ‘interpreting’ them, and the required training time will decrease.” Non-ACGME fellowships in POCUS require a department or departments to be able to budget for the expense of a fellow’s clinical salary and administrative costs for program director’s time in return for the expected benefit of an additional educator for the student and resident trainees and longitudinal growth of the program [32].

Documentation and Billing

Documentation to support billing includes the indication for the study, the type of exam, findings, and the note-writer’s interpretation of these findings as well as at least a still image, saved and retrievable [33]. Applying appropriate ICD-10 and CPT codes for the POCUN studies you most often perform will benefit from working

with your billing and coding experts to ensure the documentation will support billing. An in-depth review of documentation and billing is beyond the scope of "Nuts and Bolts" and recently published frameworks such as "Billing I-AIM" by Hughes, et al., provide an excellent and detailed discussion of POCUS billing that is generalizable to nephrology or other subspecialty practices [34]. While investigation specific to nephrology is lacking, implementation of billing for POCUS activities in a single-center experience at a tertiary care emergency department produced a net profit within one year. Niyyar and O'Neill report billing for ultrasound at an academic center performed over 20,000 point of care studies in 20+ years [13]. While it is an oft-cited worry that performing and billing for ultrasound will lead to increased liability, Niyyar and O'Neill noted no liability concerns in their time performing POCUS. This is substantiated by literature from perinatology and emergency medicine which failed to identify a single case of liability due to misdiagnosis that found no cases against internal medicine, family medicine, or pediatric physicians [35,36].

What about education and competency?

Excluded from this review thus far has been any mention of a specific educational pathway for those looking to start a POCUN program or expand their ultrasound using cohort. A one-day course is enough to light the fire, but how does one keep it stoked and challenged? Hands-on courses, online content and curricula, and even Twitter are the modern-day core content providers [1]. Robust online educational resources offer a compendium of how-to videos, literature summarized into easy-to-digest infographics, and pocket-guides for quick "just-in-time" review on a personal phone prior to scanning [37]. Coupled with short-courses, workshops held by national conferences, and mini-fellowships, the online educational resources to support the launch of a new program already exist in volumes as free, open access medical education online material (FOAMEd) [38].

How to move POCUS users engaged in a program from curious to competent remains a black box even in 2021, as there is an ongoing lack of sufficient evidence on the best methods to assess competency [39,40]. While a handful of assessments exist for specific applications, how to deploy these to bridge learners between educational and clinical scanning is also not standardized [41]. Until the evidence exists, this latitude shifts the burden of defining competency onto POCUS program directors and local expertise. The advantage to this is that it lends to a curated educational experience for the learners at a particular program. For example, some trainees may succeed in a volume-based approach (i.e., total number of scans to achieve a skill) while others succeed in a more objective skills-based approach (i.e. the skill is achieved when all boxes are checked in the pathway designed). The curricular design by the program director can be tailored to both.

Starting a POCUS Program During a Pandemic

Considering a physician needs time, creative head space, and motivation to pursue developing a new program in their department, there are more than a few ways the current pandemic might stunt this type of growth. What is lost in the limitations to networking at national conferences or in-person courses is potentially a gain for the increased physical presence of the local cohort at one's home institution. And the pandemic has shifted many national organizations to virtual formats for education with additional opportunities for online learning growing steadily. Troubleshooting the challenges of COVID-19 imposed physical distancing restrictions with the need for personal protective equipment (PPE) preservation is already underway by POCUS educators [42,43]. Ultimately the components of a well-designed program rely on local personnel to effectively collaborate in their commitment to accurate image acquisition and interpretation. Thankfully, collaboration amongst medical partners has prevailed during COVID-19, and sets a precedent for a future anticipated to include other emerging pathogens [44,45].

Conclusion

These Nuts and Bolts can build a program in many different ways. There is no specific timeline to follow to engage potential teammates. A starting program in a site with three nephrologists well-trained in POCUN with strong administrative support and easy collaboration across departments would be expected to progress beyond the basics of program development rather quickly. On the other hand, a solo aficionado working to increase their skills through a national certificate program while simultaneously building the scaffolding for a well-designed program could be expected to need several years to accomplish the network described above. Invariably, there will be more that is unexpected than is planned, but that is the allure of building something from scratch. With a plan for each of the basic pieces described above, a new program will have solid footing on which to start.

Disclosures

None.

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FEB 2022 vol. 07 Kidney | POCUS J | 94

Bedside Assessment of the Kidneys and Bladder Using Point of Care Ultrasound

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History and Background

Given the contrasting echogenic characteristics of the urinary system and their easily identifiable distortion in response to numerous pathologic processes, the sonographic examination of the kidney and bladder can provide a wealth of clinical information [1, 2]. Although performed for decades as a referral and comprehensive radiologic study, improvement in the cost and performance of portable ultrasound devices has now made point of care ultrasound (POCUS) accessible to a growing number and variety of healthcare providers. The purpose of this review is to describe the technique and benefits of using POCUS to evaluate the kidneys, ureters, and bladder in common clinical scenarios.

POCUS gives clinicians more diagnostic information at the bedside than they can gather using traditional physical examination techniques, allowing them to expedite further diagnostic tests and provide more targeted and timely management. For example, while a distended bladder may be palpated on physical exam, the positive likelihood ratio for palpation of 600 mL of urine is only 1.62 when using POCUS as the criterion standard [3]. Furthermore, POCUS can identify causes of bladder outlet obstruction, such as an obstructed or malpositioned urinary catheter or a bladder mass, thus informing appropriate management. While referral ultrasound is the standard against which POCUS is compared, it is not always immediately available due to resources or patient condition. POCUS can be performed at the bedside within minutes, does not subject patients to radiation, and can be easily repeated to gauge the progression of pathology or impact of interventions [4].

Ultrasound machines are becoming more portable and inexpensive, placing them in the hands, and pockets, of more clinicians. While pocket ultrasounds generally have inferior resolution compared to full platform machines, particularly in obese patients, a 2017 study comparing pocket POCUS performed by urology residents to standard sonographer-performed ultrasound for presence of hydronephrosis resulted in a Cohen's kappa coefficient of 0.62, suggesting moderate agreement [4, 5]. A similar and more recent study showed moderate to strong agreement (κ = 0.61-0.80) for measurement of kidney length and presence of cysts or hydronephrosis [4]. These studies support the use of pocket devices to improve diagnosis at the bedside while cautioning against overconfidence in it as a standalone imaging modality.

Technique and normal sonographic appearance of the kidney

Ultrasound evaluation of the urinary system consists of evaluation of the kidneys, bladder, and the ureters near the ureteropelvic (UPJ) and ureterovesical (UVJ) junctions, typically using a 2 - 5 MHz transducer in B-mode with the patient in a supine or decubitus position [1, 2]. While a phased array transducer fits well between ribs, the large footprint of the curvilinear transducer allows for easier longitudinal measurement of the kidneys and bladder [2]. Color Doppler techniques can be used to evaluate arterial inflow and venous drainage [6-9]. The right kidney can be evaluated through an acoustic window provided by the liver, typically anteriorly or along the mid-axillary line. The left kidney is approximately 1 vertebral level higher than the right, can be visualized through an acoustic window provided by the spleen, and typically requires a more posterior approach [10]. The marker on the transducer should initially be oriented superiorly and then slowly rotated 15 - 30 degrees (counterclockwise for the right kidney and clockwise for the left kidney) to obtain the true longitudinal plane of the obliquely positioned kidneys, since the inferior poles are more anterolateral [2]. Measurement of kidney length should be obtained multiple times and the longest measurement recorded. Rotation of the transducer 90 degrees counterclockwise from the longitudinal plane yields the short axis view. Fanning from the superior pole to inferior pole in the transverse plane ensures no pathology is missed. To aid in visualization, a seated position can help move the left kidney below the costal margin as can a prolonged inspiratory breath-hold [10, 11].

The normal kidney has a characteristic ultrasonographic appearance (Figure 1, Video S1). Typically, a layer of white perinephric fat surrounds the darker cortex of the kidney. The cortex appears more echogenic than the medulla, while appearing hypo- or isoechoic compared to the liver and hypoechoic to the spleen [10, 12, 13]. The increased echogenicity of a cirrhotic liver alters this relationship, decreasing the sensitivity of detecting abnormal right kidney pathology. The tips of the pyramids, oriented toward the renal sinus, form the papilla that excrete urine into minor calyces, which fuse to form major calyces and then subsequently the renal pelvis. In younger patients the pyramids in the medulla can be mistaken for renal cysts due to their relative hypoechogenicity [14]. The renal sinus contains the collecting system, the large renal vessels, and perihilar fat. When urine is draining normally, the renal sinus appears hyperechoic on ultrasound owing to the predominant echogenicity of fat [11, 14, 15].

Emamian et al. showed in a study of 665 healthy volunteers that the measurement of renal length alone is more practical than the calculation of renal volume from ultrasound measurements of kidney length, width, and thickness and provided reference values from their large data set [16]. The volume and length of the right kidney is typically smaller than the left. The authors grouped volunteers and their kidney measurements by chromosomal sex. In adults, the median length of the right kidney in females is 10.7 cm (range 9.5 - 12 cm) and in males, 11.2 cm (range 10.1 - 12.4 cm). The median length of the left kidney in females is 11 cm (range 9.4 - 12 cm) and median length in males is 11.5 cm (range 10.4 - 12.6 cm). The authors noted a small but acceptable difference between supine and prone measurements [16].

Ultrasonographic appearance of chronic kidney disease

Renal length, cortical echogenicity, and cortical thickness can give clues to the chronicity of medical renal disease. Keeping in mind that people of shorter stature tend toward the lower range of kidney length, kidneys smaller than the lower end of the ranges described above suggest chronic kidney disease (CKD) [16]. Certainly, a length of $\leq$ 9 cm is suspicious [17]. As mentioned previously, the transducer needs to be rotated slightly obliquely to capture the longest orientation of the kidney as failure to do so will lead to an underestimation of kidney length. Regardless of the cause of the pathology, the cortex becomes more echogenic with respect to the appearance of the nearby liver or spleen with prolonged pathology [11] (Figure 2 and Video S2). Ideally, the thickness of the cortex should be measured from the base of the pyramids, if visible, to the capsule. If the pyramids are not easily visualized, the parenchyma can be measured from the hyperechoic renal sinus to the capsule [11]. Normal cortical thickness is 7 - 10 mm and normal parenchymal thickness is 15 - 20 mm [18]. In general, short kidney length with cortical thinning is suggestive of advance CKD; however, these sonographic signs should be considered in totality and in context of historical clues as hyperechogenicity can be seen in the setting of acute tubular necrosis. Additionally, POCUS can readily uncover underlying cystic disease associated with CKD (as discussed further below).

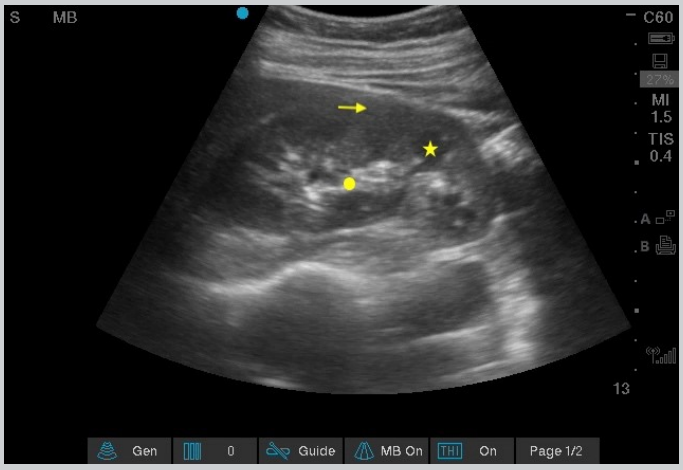

Figure 1. Normal right kidney in longitudinal view. Arrow: cortex, star: hypoechoic medullary pyramid, dot: renal sinus with hyperechoic fat. Video S1 can be found in supplementary material.

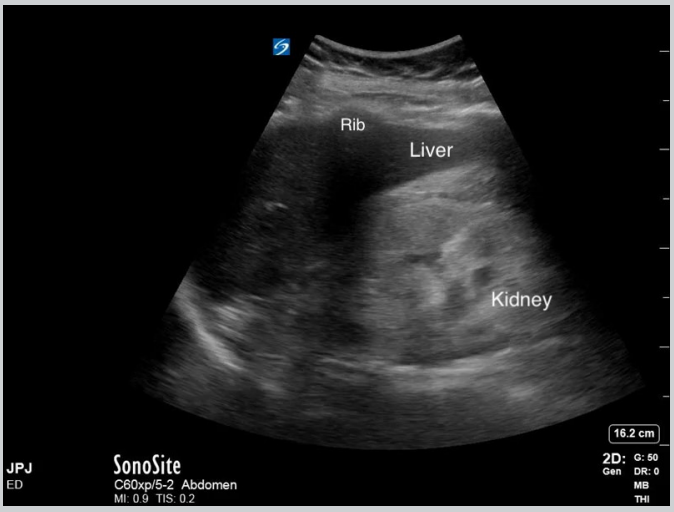

Figure 2. Hyperechoic kidney seen in a patient with chronic kidney disease. Note that the kidney echogenicity is described relative to the liver parenchyma. Video S2 can be found in supplementary material.

Ultrasonographic appearance of obstructive kidney disease

Acute kidney injury (AKI) due to obstruction can be suggested by the finding of hydronephrosis on POCUS. Typically, the collecting system and ureters are actively drained of urine, such that the predominant signal in the renal hilum is hyperechoic due to sinus fat. In the setting of obstructive uropathy, distention of the collecting system with anechoic urine (i.e., hydronephrosis) can be readily detected by ultrasound. Hydronephrosis is graded as mild when only the renal pelvis and/or major calyces are dilated, moderate when both major and minor calyces appear dilated (the bear claw appearance seen in Figure 3 and Video S3), and severe when there is parenchymal effacement of the cortex [15] (Figure 4 and Video S4). Hydronephrosis can be distinguished from hypoechoic pyramids by the presence of interdigitating hyperechoic sinus fat between the dilated calyces, and distinguished from renal vasculature with the use of color Doppler, which should show no flow in the collecting system [15]. Mild hydronephrosis may be seen in non-obstructed states such as pregnancy, full bladder, vesico-ureteral reflux, urinary tract infection, and brisk diuresis [19].

Figure 3. Moderate hydronephrosis with the classic bear claw appearance caused by dilation of the major and minor calyces. Video S3 can be found in supplementary material.

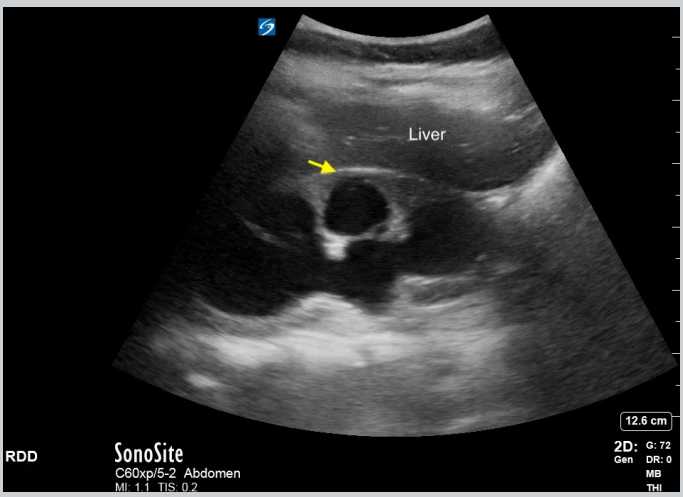

Figure 4. Severe hydronephrosis with ballooning of the calyces and effacement of the renal cortex (yellow arrow). Video S4 can be found in supplementary material.

Numerous studies have evaluated the use of POCUS for detection of hydronephrosis with sensitivities and specificities ranging from 72 - 96% and 59 - 96%, respectively [20-27]. A great majority of studies to date have focused on patient populations presenting with flank pain or suspicion for renal colic with the bedside ultrasounds performed by emergency physicians [20, 21, 24-28]. Nixon et al. studied POCUS performed by 28 generalists in rural New Zealand hospitals as part of routine practice and found a high sensitivity (90%) and specificity (96%) for hydronephrosis, which suggests POCUS evaluation for hydronephrosis may be feasible in other settings [22]. Ensuring adequate intravascular volume with appropriate IV fluids augments the detection of hydronephrosis by POCUS by promoting urine production and subsequent dilation of the collecting system [29].

Technique for bladder imaging and measurement

The presence of hydronephrosis should prompt careful evaluation of the bladder. The bladder is imaged by placing the transducer in the anterior midline, directly above the pubic symphysis. With the transducer in a transverse plane, fanning superiorly to inferiorly allows for measurement of maximal width (Figure 5a and Video S5a). The transducer is then rotated 90 degrees to obtain a longitudinal view and provide for measurement of the bladder's anterior-posterior depth and cranio-caudal height [30] (Figure 5b and Video S5b). Several formulae allow for estimation of bladder volume based on these measurements with similar degrees of accuracy, the most common being the prolate ellipsoid formula:

Volume (mL) = depth x width x length x 0.52 [31].

While imaging the bladder, the presence of ureteral jets can be captured by using the color or power Doppler mode with a small window and low color velocity while over the UVJ which appear as papules in the posterior bladder wall [14, 15]. In addition, the UVJ should be evaluated for the presence of stones. While evaluating the bladder, avoid excessive far field gain as posterior acoustic enhancement can easily obscure findings posterior to the bladder such as hydroureter, ureteral stones, and shadowing from stones or free fluid [10].

Advanced POCUS renal evaluation for AKI

In patients presenting with kidney failure of unknown chronicity, a combination of small kidney length, increased echogenicity, and decreased cortical thickness can suggest CKD. It is important to note, however, that hyperechogenicity of the parenchyma can be seen in both AKI, where it may be due to inflammation or proteinaceous casts, as well as in CKD, where increased signal may be due to fibrosis [17, 19]. Therefore, while hyperechoic renal parenchyma signals disease with 96% specificity and 67% positive predictive value, it gives no specific indication regarding the chronicity, severity, or etiology of intrinsic renal disease [19]. Furthermore, since glomeruli only make up 8% of the cortex, even biopsy proven severe glomerular disease may not cause ultrasonographic changes [17].

More advanced POCUS techniques for investigation of AKI include interrogation of renal perfusion and drainage using Doppler-based modalities to calculate the renal resistive index (RRI) and venous impedance index (VII), respectively [7, 8, 32-35]. Using pulsed-wave Doppler interrogation of the interlobar arteries, the RRI is calculated using the formula:

RRI = (peak systolic velocity - end diastolic velocity) / (peak systolic velocity)

A greater difference between peak systolic velocity and end diastolic velocity leads to a higher RRI and reflects resistance to blood flow [19]. Normal RRI ranges between 0.56 and 0.66 and was found to be > 0.7 in only 3% of healthy kidneys [36]. While an advanced POCUS skill, two studies have shown that novice and intermediate POCUS users can obtain RRI measurements with good to excellent interobserver reproducibility compared to expert sonographers with only 4 - 6 hours of training [32, 34]. Similarly, venous drainage from the kidneys can be assessed using pulsed-wave Doppler in the interlobar veins. If the intra-renal venous flow pattern is biphasic, VII can be calculated using the same formula as above [35]. For both RRI and VII, averages should be calculated from multiple measurements.

The clinical utility of RRI, intra-renal venous flow pattern, and VII remain unclear at this time. A 2015 meta-analysis of 449 patients with AKI suggested that RRI > 0.7 predicts persistence of AKI beyond 72 hours, although the authors noted significant heterogeneity of the studies and recommended further large prospective studies [6]. Subsequently, Oliveira et al. prospectively found that RRI between critically ill patients without AKI and those with transient AKI were not statistically different but patients with persistent AKI had statistically higher RRI compared to the other two groups [37]. Conversely, Darmon et al. showed that while patients with AKI had increased RRI compared to those who did not, RRI was poorly predictive of persistent AKI [7]. Wiersema et al. found that there was no significant difference in measurements of both arterial and venous flow in critically ill patients with or without AKI [35]. Similarly, Spiegel et al. found that abnormalities in interlobar venous flow patterns were not associated with increased risk of adverse kidney events [8]. Further study

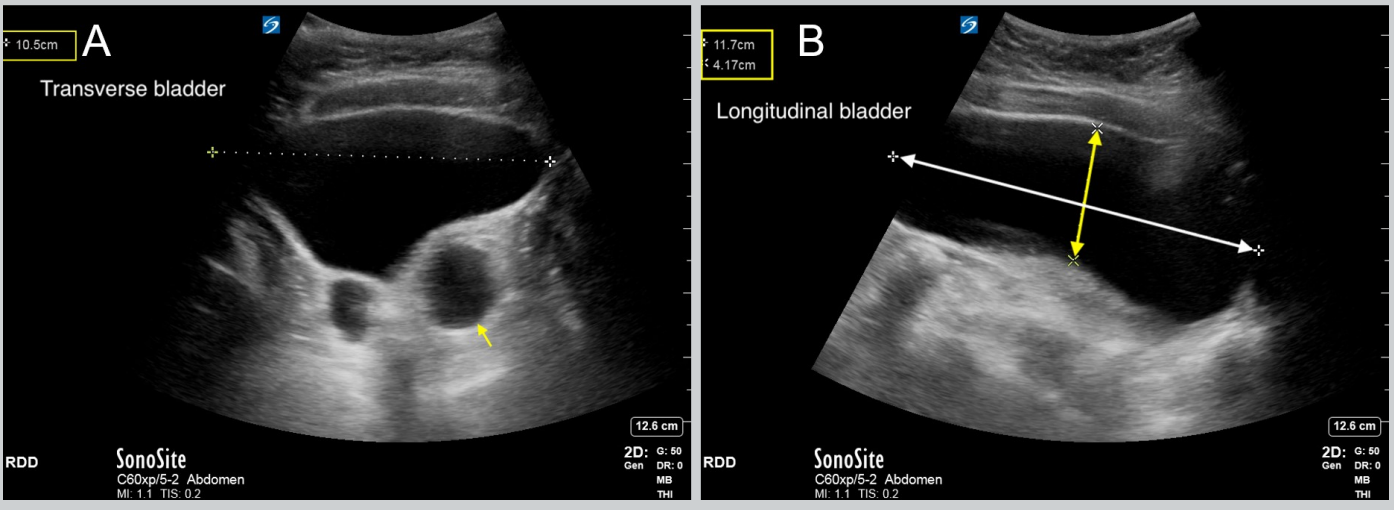

Figure 5. A) The width of the bladder is measured in the transverse view. In this image, the width is approximately 10.5 cm. Also seen in this image is a dilated left ureter as it enters the bladder at the UVJ (yellow arrow). Video S5a can be found in supplementary material. B) The depth (double ended yellow arrow) and height (double ended white arrow) of the bladder is measured in the longitudinal view. In this image, the depth is approximately 4.2 cm and the height is 11.7 cm. Using the width measurement in the above figure, this patient's estimated bladder volume is 10.5 cm x 4.2 cm x 11.7 cm x 0.52 = 268 mL. Video S5b can be found in supplementary material.

of systemic congestion assessment is underway that incorporates renal perfusion and drainage with inferior vena cava (IVC) investigation and Doppler interrogation of the portal and hepatic veins [9].

POCUS in the evaluation of renal colic

Renal colic is the term used to describe the abrupt and severe flank and low back pain caused by acute obstruction and distension of the ureter and renal pelvis [29]. POCUS is a useful aide in the management of renal colic, allowing for the direct visualization of stones in some cases or providing indirect evidence of their presence by detecting signs of urinary tract obstruction such as hydronephrosis or absence of ureteral jets [38].

Direct visualization of calculi within much of the course of the ureter can be difficult as overlying bowel gas and adjacent bony structures leads to poor insonation. As a result, only stones near the UPJ or UVJ are amenable to sonography, leading to only about 64% of stones being in the field of view afforded by POCUS [39] (Figures 6a and 6b and Videos S5a and S5b). Furthermore, ultrasound has a sensitivity of 16% for stones smaller than 7 mm and 75% for stones $\geq$ 7 mm [40]. This limited field of view coupled with the poor sensitivity of ultrasound for small stones makes POCUS of limited value for detecting renal calculi (sensitivity of 24% for all stones compared to computed tomography) [40]. On the other hand, the high specificity (98%) and positive predictive value suggests that calculi identified on ultrasound correspond to calculi visualized on computed tomography (CT) and therefore is an appropriate technique to rule-in the presence of stones [40]. Even without direct visualization of stones, when initial clinical suspicion is high and a strong competing diagnosis is lacking, the presence of hydronephrosis on POCUS is supportive of renal colic.

Despite the limitation in direct stone visualization, the presence and grade of hydronephrosis can help to inform the management of patients presenting with renal colic. Patients with no hydronephrosis are at low risk for hospitalization or urologic intervention [41]. Moderate to severe hydronephrosis has poor sensitivity but 94% specificity for the presence of a stone [38]. Patients with renal colic and moderate or severe hydronephrosis on POCUS are more likely to require a urologic intervention [38]. The improved sensitivity of diagnosing larger stones when a high degree of hydronephrosis is present may be helpful for stratifying a patient's risk for failure of expectant management of urolithiasis and support a clinician's choice to pursue further imaging or urologic consultation if symptoms do not resolve after a trial of passage [38]. Limitations of using hydronephrosis in the diagnosis of renal colic is that a proportion of renal stones do not cause hydronephrosis, and the presence of hydronephrosis does not rule out alternative diagnosis for abdominal pain [38]. Of note, if bilateral hydronephrosis is seen in the investigation of renal colic, other etiologies, associated with a lower urinary tract obstruction, should be considered although simultaneous ureteral obstruction is possible [42]. Patients with renal colic can be severely volume depleted due to associated nausea and vomiting, leading to a false-negative exam for hydronephrosis. Sensitivity for identifying hydronephrosis can be increased by appropriate volume resuscitation prior to imaging [29].

Color Doppler ultrasonography (CDU) at ureterovesical junctions can be used to look for ureteral jets of urine flowing into the bladder which serve as a surrogate for ureteral flow. In combination with the presence of hydronephrosis, ureteral jet asymmetry with an absent or

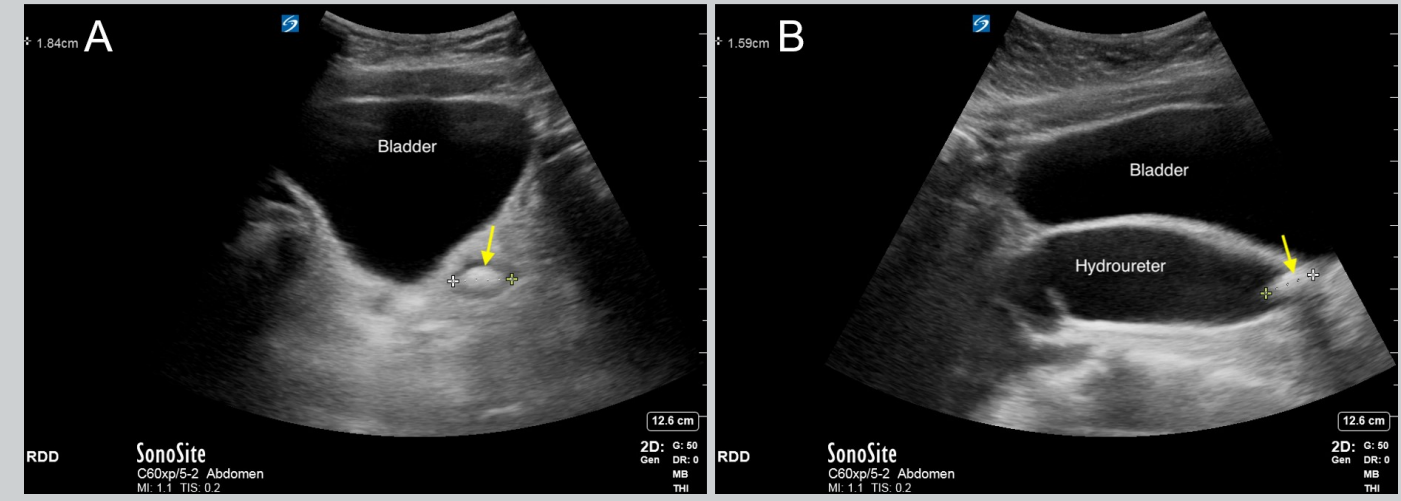

Figure 6. A) 1.8 cm stone in the UVJ (yellow arrow), seen in transverse. Video S5a can be found in supplementary material. B) Stone in the UVJ (yellow arrow), seen in longitudinal and measuring approximately 1.6 cm. Note that the ureter is severely dilated. Video S5b can be found in supplementary material.

weaker jet lateralizing to the side with symptoms of renal colic can be seen in obstructive ureterolithiasis. Notably, bedside ureteral jet evaluation does not significantly contribute to prediction of patient outcomes, including need for hospitalization or urologic procedure. It can, however, be used by clinicians to assess the need for additional advanced imaging [43].

CDU twinkling artifact is a form of intrinsic noise when insonating certain rough reflective surfaces (like urolithiasis), and appears as a discrete focus of alternating color signals behind an echogenic surface [44]. The presence of a twinkle may indicate the presence of nephrolithiasis. In a recent meta-analysis, the pooled sensitivity of this sign was 88% with a range of 40-100% and the pooled specificity was 79% with the same range, suggesting significant heterogeneity [44].

According to a 2018 meta-analysis, accuracy of POCUS for the diagnosis of nephrolithiasis is modest relative to CT scan, with a pooled sensitivity and specificity of 70.2% and 75.4%, respectively [38]. The decision to pursue further imaging after POCUS should be informed by a combination of history, physical exam, and urine analysis, in addition to POCUS findings. Encouragingly, studies comparing ultrasound versus CT in the initial management of renal colic show no difference in complications, adverse events, pain scores, or hospitalizations [45].

Utility of POCUS in urinary tract infection:

Although pyelonephritis can appear as areas of increased or decreased echogenicity relative to the surrounding kidney and Doppler evaluation can demonstrate decreased vascularity due to corresponding tubular ischemia, the sensitivity of US for detection of pyelonephritis is low [46]. The main utility for POCUS in the evaluation of patients with pyelonephritis is the timely identification of underlying obstructive uropathy and complications such as pyonephrosis, abscess, or emphysematous pyelonephritis, which can expedite appropriate treatment. Chen et al. found retrospectively that POCUS detected significant abnormalities such as stones, hydronephrosis, or abscesses in 39.6% of patients presenting with acute pyelonephritis [47]. The detection of significant findings increased to 56.6% of patients with the addition of abdominal radiography which was nearly equal to the 58.8% of patients found to have significant abnormalities by CT [47]. Use of POCUS in this study diverted 34.3% of patients to receive interventions such as abscess drainage, stone removal, nephrostomy, and nephrectomy [47].

Evidence of emphysematous pyelonephritis typically appears as a high amplitude/echogenic focus associated with distal “dirty shadowing” or low-level echoes and reverberations caused by the near total sound reflection at the tissue-air interface, distinct from the echo-free shadow formed by calculi [48, 49]. The ultrasonographic appearance of renal abscesses can range from hyper- to hypoechoic focal masses or cystic structures, potentially with posterior acoustic enhancement [46]. The absence of vascularity helps to distinguish abscesses from potential malignant findings, although occasionally mobile debris may be seen that can be misinterpreted as vascular flow on Doppler [46, 50]. If air is present within the fluid collection, a ring-down artifact may be present [51]. It should be noted that while POCUS can suggest emphysematous changes or abscess, the most recent recommendation of the American College of Radiology maintains CT as the imaging study of choice for patients presenting with pyelonephritis and either a complex presentation or failure to respond to antibiotics [52].

Mimics, masses, and variants

Renal cysts are common and can be found in 24 - 47% of the general population, with a higher prevalence in the aging population [53]. Cysts appear as circular or ovoid shaped, typically anechoic structures that demonstrate posterior acoustic enhancement [10, 15]. Although commonly located in the periphery of the kidney, cyst can be found in the sinus where they can be mistaken for hydronephrosis. Because ultrasound can accurately detect cysts larger than 0.5 cm, POCUS practitioners will encounter cysts and must be able to characterize and distinguish them from similar lesions, such as hydronephrosis, solid masses, and abscesses [54]. While hydronephrosis progresses from the renal pelvis to the major and minor calyces and then to the cortex, cysts are cortical or parapelvic and do not follow this anatomic pattern [55, 56]. Most cysts are asymptomatic. However, ruptured cysts can cause pain and hematuria and cortical cysts may grow large enough to stretch the renal capsule [56]. Obstruction is another possible, though rarer, complication [56].

While it should be noted that the Bosniak classification of renal cysts was created to apply to lesions seen on renal CT, the 2019 version of the Bosniak classification does allow diagnosis of simple cysts—Bosniak 1—by ultrasound if the structure is round or oval, thin-walled, anechoic, not septated, and displays posterior acoustic enhancement [57]. The posterior acoustic enhancement provides reassurance that the cyst contains simple fluid (Figure 7 and Video S6). These simple cysts need no further evaluation [1]. All other cystic lesions should be referred for more definitive imaging [57].

The most common cystic kidney diseases are autosomal dominant polycystic kidney disease (ADPKD) and acquired cystic kidney disease (ACKD). Both diseases are characterized by multiple bilateral kidney cysts.

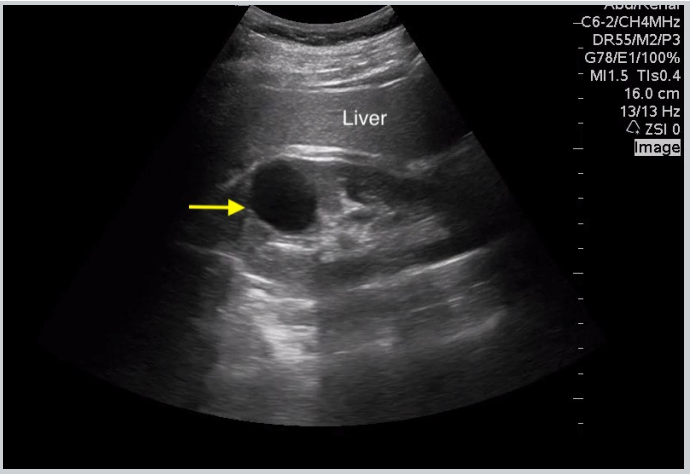

Figure 7. Simple renal cyst in right kidney (yellow arrow). Note the posterior acoustic enhancement. Video S6 can be found in supplementary material.

Figure 8. Autosomal dominant polycystic kidney disease causing numerous cysts in the right kidney and liver.

However, while ADPKD can progress to end stage kidney disease, ACKD increases in prevalence the longer patients have advanced CKD or end stage kidney disease–reaching a prevalence of almost 90% in patients who have been on dialysis for 5 - 10 years [58, 59]. POCUS can easily detect two features that distinguish ADPKD and ACKD–renal size and extra-renal involvement. ADPKD invariably results in enlarged kidneys while kidneys with acquired cystic disease are frequently smaller, with cortical thinning typical of CKD [60]. In patients with ADPKD, Bhutani et al. showed that kidney length measured by ultrasound had an area under the receiver operating curve (AUROC) similar to magnetic resonance imaging (0.87 versus 0.86, respectively) for predicting CKD stage 3 within 8 years, using a cutoff of 16.8 cm on ultrasound [61]. Finally, given their proximity to the kidneys, extra-renal manifestations of ADPKD in the liver and spleen are easy to assess with POCUS. Liver cysts are especially common–affecting over 80% of patients with ADPKD at 30 years old [62] (Figure 8). Distinguishing ADPKD from ACKD is important as ACKD is a pre-malignant condition [1].

Solid renal masses may have cystic components but are mostly echogenic. The most common tumor is renal cell carcinoma, which is typically found in the periphery and may be somewhat difficult to identify since they are usually isoechoic and are poorly differentiated from the surrounding parenchyma [11]. Other malignant tumors include transitional and squamous cell carcinomas, adenocarcinomas, and lymphoma [11]. The most common benign mass is angiomyolipoma (AML), which is distinguishable from RCC if fat is a major component as it will be hyperechoic. However, it is important to remember that AML may also have minimal fat and therefore appear similar to RCC on POCUS [63]. Overall, the sensitivity of ultrasound is inadequate for detection of RCC and CT imaging or alternatively MRI remain the preferred imaging modalities.

Other common ultrasonographic findings easily mistaken for neoplasms may be developmental variants, infections, or vascular abnormalities [64]. The dromedary hump is one such common normal variant seen on POCUS (Figure 9a and 9b). It is a protuberance on the lateral aspect of the left kidney that resembles a camel's hump that is thought to be a result of being molded by the spleen [65, 66]. Hypertrophied column of Bertin is another common variant that is characterized by a prominent, wide bridge of cortical parenchyma between pyramids that appears to bulge into the renal pelvis and mimics a mass [64] (Figure 10). Both variants can be recognized by their position in the kidney and their similarity in appearance with the rest of the normal cortical parenchyma. Junctional parenchymal defects occur due to partial fusion of fetal renunculi and may be mistaken for a hyperechoic lesion or scar [67] (Figure 11 and Video S7). Finally, persistent fetal lobulations are caused by indentations that characteristically overlie the spaces between the pyramids and may lead to an appearance of multiple mass-like projections in the cortex [64]. Previously discussed infectious processes, such as focal pyelonephritis and abscesses can also mimic neoplastic processes. Finally, vascular defects, the most common being arteriovenous malformations, may mimic tumors as well. These may appear anywhere in the kidney and will look similar to malignant tumor on CT as there will be contrast enhancement. However, color Doppler enhanced POCUS will show that this "tumor" is a collection of blood vessels without parenchyma [64]. Despite the ability of

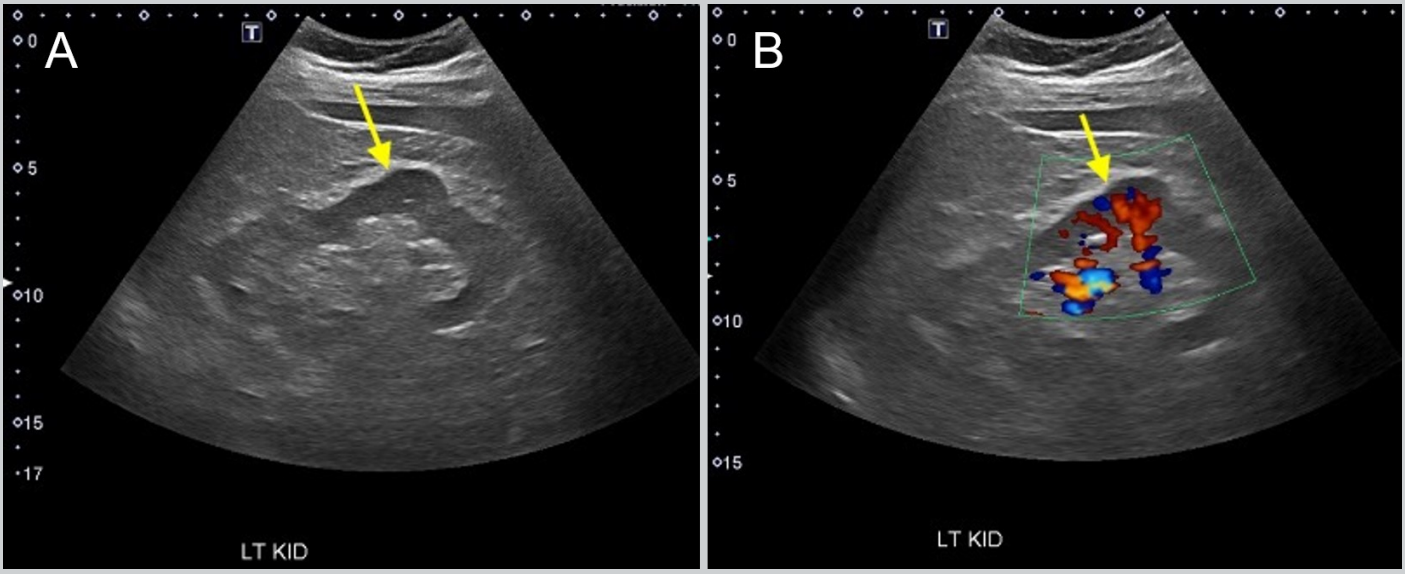

Figure 9. A) Dromedary hump (yellow arrow) of the left kidney. Image courtesy of Dr. Abhilash Koratala. B) Dromedary hump (yellow arrow) of the left kidney. Color flow Doppler illustrates normal blood flow into this normal cortical parenchyma. Image courtesy of Dr. Abhilash Koratala.

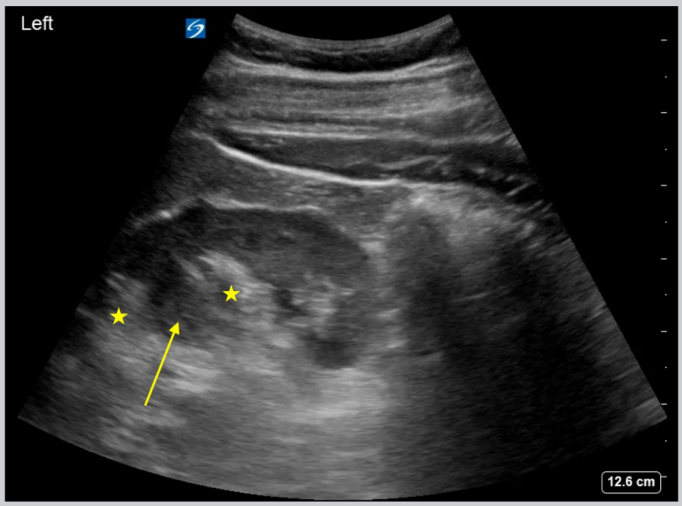

Figure 10. Hypertrophied column of Bertin (yellow arrow). Note that the hypertrophied cortical parenchyma appears to cleave the fat in the renal pelvis (yellow stars). Image courtesy of Dr. Kylie Baker.

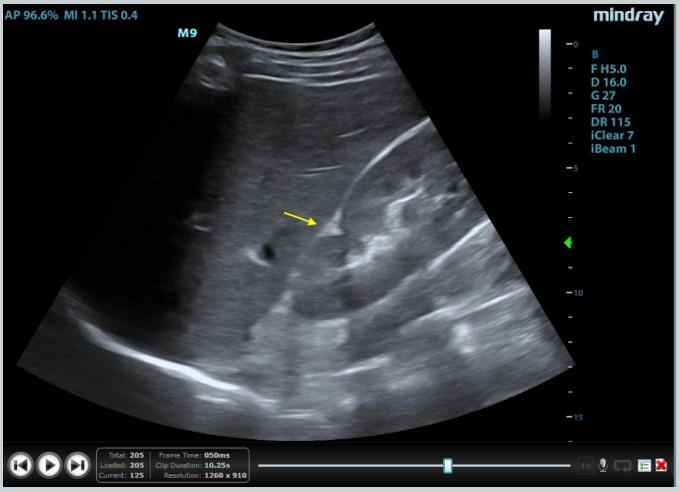

Figure 11. Junctional parenchymal defect (yellow arrow). Video S7 can be found in supplementary material.

POCUS to differentiate some of these neoplastic mimics, any beyond a clear simple cyst or common anatomical variant requires referral.

As more POCUS exams are performed, more incidental renal findings will be found. Responsible practice of POCUS involves recognizing and reporting these findings. A study of 1,452 focused assessment with sonography for trauma (FAST) exams in 2 academic emergency departments showed that incidentalomas were found in 9.4% of patients and the most common incidental findings were renal cysts [68]. Of those, only 22.6% were documented and only 6 of 70 discharged patients had documentation that they were notified of the incidental finding or were referred for follow-up [68]. A small case series of incidental renal cell carcinomas seen in an ambulatory cardiology clinic suggests that widespread adoption of POCUS coupled with robust referral may result in early detection and improved outcomes [69].

POCUS Training

POCUS is rapidly diffusing throughout general internal medicine and its subspecialities throughout the training

spectrum from undergraduate and graduate medical education to subspecialty fellowship training and continuing medical education [70]. Over half of medical schools surveyed in 2014 included POCUS in their curriculums and that number has undoubtedly increased since then [71]. The Alliance of Academic Internal Medicine (AAIM) released a position statement in 2019 describing the barriers to creating a POCUS curriculum and offering a model for longitudinal training [70]. That same year, POCUS became a “mandatory skill” for residents in the Netherlands [72]. A national survey showed that these residents thought renal ultrasound was the second most useful core application, after IVC ultrasound. The most important barrier they identified was an insufficient number of experts to teach the curriculum [72].

Nephrologists who are expert at not just renal and bladder ultrasound, but who can also integrate focused cardiac, lung, and vascular ultrasound are in a good position to teach all levels of learners. Nephrology fellowships are beginning to integrate POCUS into training, and a model curriculum has been proposed [65]. Introductory courses and workshops are increasingly being offered at society conferences [1]. Those who wish to pursue competency in renal and bladder sonography may pursue certification through the American Society of Diagnostic and Interventional Nephrology. For more comprehensive training, the Society of Hospital Medicine and the American College of Chest Physicians offer a certificate of completion in acute and critical care POCUS.

Conclusions and Future Direction

The use of POCUS for the assessment of urinary system pathology is poised to greatly expand in the coming years given the declining cost and improving performance of the ultrasound equipment itself, the proliferation of POCUS training at all levels of medical education, the significant savings it affords compared to traditional types of imaging, and most importantly the additional clinical information it provides at the bedside. It is unknown at this time if the previous sensitivities and specificities found in studies of traditional or emergency provider performed ultrasonography will be recapitulated by members of other specialties; however, one would expect that the ultimate performance characteristics will depend largely on the operator’s knowledge and experience, therefore, the early introduction of urinary system focused POCUS training along with incentivization for its use will likely lead to better performance and, in turn, improved patient care. For now, the utility of POCUS in the workup of kidney injury to quickly identify obstruction in the form of hydronephrosis and/or bladder distention and evidence of chronic renal disease is clear. Although POCUS may not supplant more advanced imaging for some indications given the factors mentioned above, the frequency with which it is able to preempt patients from requiring those forms of imaging will continue to grow in the coming years.

Disclosures

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Review

Point of Care Ultrasound of the Hemodialysis Vascular Access

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Abstract

The effectiveness of hemodialysis is completely dependent on the quality of the patient's vascular access; thus, appropriate assessment of ateriovenous fistulas and grafts is of critical importance. Point of care Ultrasound (POCUS) can be an additional useful skill at the bedside for assessment of the hemodialysis vascular access. In this paper we discuss the basic terminology and techniques that can be employed in the POCUS exam of vascular accesses. We also delineate the current recognized criteria for access maturation and common issues that can be diagnosed with the support of POCUS.

Introduction

Hemodialysis is the most prevalent mode of renal replacement therapy in the United States [1]. For hemodialysis to be an effective treatment relies heavily on the quality of the patient's vascular access. To promote the success of a patient's vascular access it is required that the clinician is well versed in maturation assessment, strategies for cannulation, monitoring, and diagnosis of potential access related issues and complications. While clinical signs and physical exam strategies are extremely important, point-of-care ultrasound (POCUS) is an additional valuable skill in order to provide optimal vascular access care. A focused ultrasound of the vascular access with a portable inexpensive device can provide important information in relatively little time.

In this review we aim to discuss the clinical applications and describe the different techniques involved in POCUS assessment of vascular access in hemodialysis patients.

For POCUS of the vascular access, a linear phased array probe is preferred, as the focus is mostly in superficial structures. The examiner will use B mode, color Doppler, and pulsed-wave Doppler modes (Figure 1).

B-mode is used to identify the access and other surrounding structures such as blood vessels or fluid collections. Color Doppler is used to assist and confirm findings on the B-mode and to monitor the patency of the access. Examples include showing the presence of a non-occlusive thrombus, detection of aneurysms and pseudoaneurysms, and identifying active bleeding. Doppler mode is used to measure blood flow.

When evaluating any access either by physical exam and POCUS, the operator should focus on 3 elements: inflow, conduit, and outflow. Inflow segment includes inflow artery, arterial anastomosis, and juxta-anastomotic segment. The body of the fistula or graft itself is the conduit, also termed the "stick zone"—the segment that is being cannulated. The outflow segment starts at the venous anastomosis in a graft and at the outflow veins beyond the cannulation zone in an AV fistula. In the text, when we say "longitudinal axis" we will be referring to the view in which the probe is parallel to vessel/access. When we say "transverse axis" we will be referring to the view in which the probe is perpendicular to the vessel/ access. See Figure 2 for reference below.

Access Mapping

Pre-operative ultrasound mapping is recommended before every access creation. We will not review the vessel mapping done to guide access choice and surgical planning. We will focus on the post creation mapping of the access. The intent of this type of mapping is to determine maturation, help the dialysis unit with early cannulation attempts, and assist when difficulty with cannulation is encountered.

By using POCUS in conjunction with one's physical exam it is possible to mark the course or path of the access with a skin marker. Markings should include the size and depth at different points in addition to identify branch veins. Such markings will make the cannulation process easier and often increase the usable area of the access [2]. Additional papers have also reported a shorter time from surgery to first successful access cannulation via the use of POCUS for mapping and, thus, decreasing the need for initial placement and duration of use of tunneled dialysis catheters [2]. Finally, the use of POCUS prior to cannulation has also been shown to improve the patient's experience, decreasing the need for multiple attempts at cannulation and infiltration events [3].

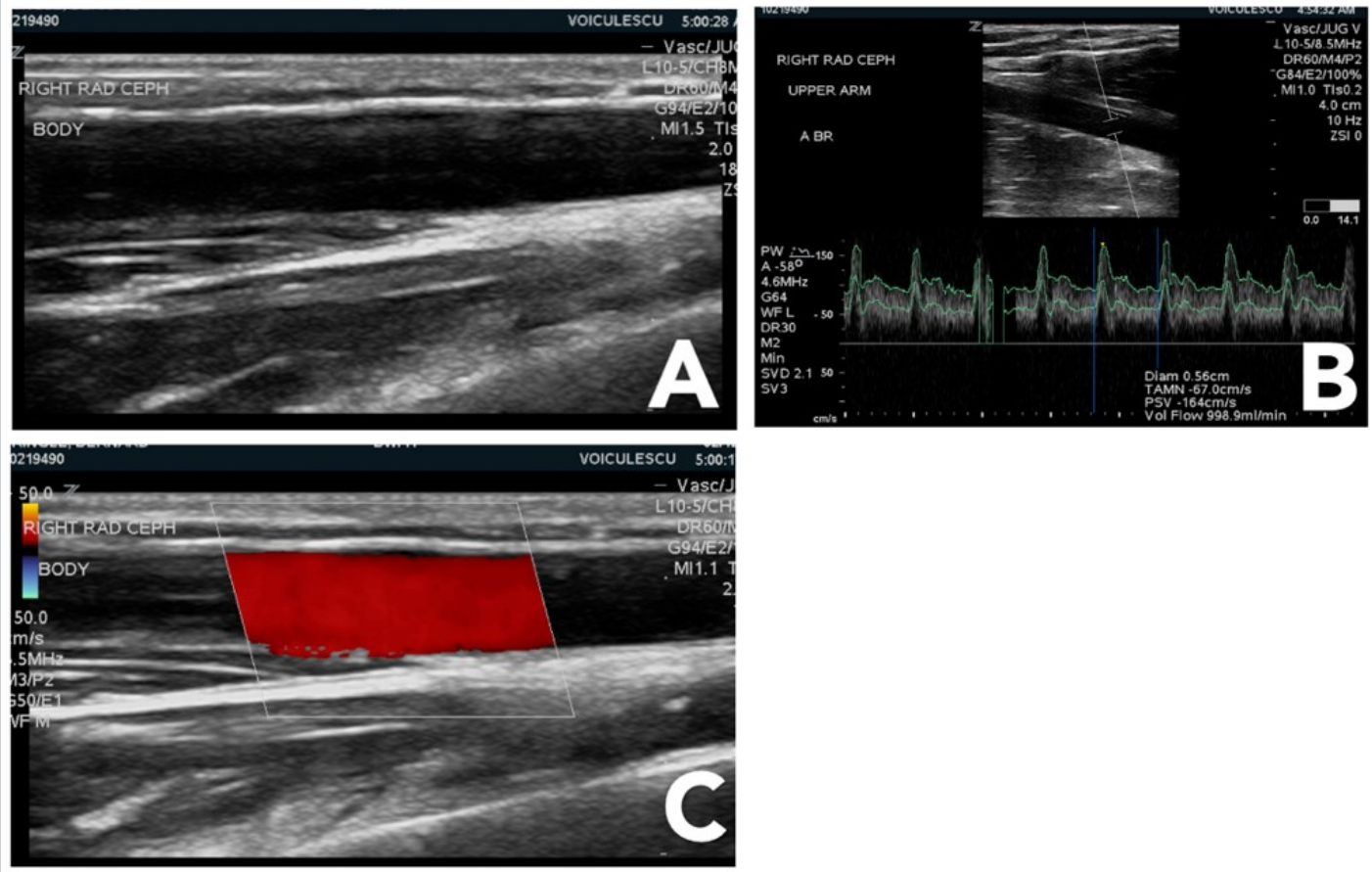

Figure 1. Ultrasound modes used for vascular access examination. A) B-mode (brightness); B) D-mode (Doppler); C) C-mode (color); Figures courtesy of Dr. Adina Voiculescu.

In order to map a fistula, the patient should ideally be positioned at 45º and the operator should have access to the whole arm [4]. The operator should scan the arm starting by focusing on the arterial inflow area in a transverse position with the ultrasound in B-mode. The two most commonly used arteries for vascular access are the radial artery (distal or proximal) and the brachial artery. The operator should follow the trajectory of the arterial vessel until the antecubital fossae if the access is distal radial (with anastomosis close to the wrist). If the access is brachiocephalic, brachiobasilic, brachio-brachial, or proximal radial (just below the elbow), the vessel should be followed until the axillary area [5]. On the ultrasound monitor, the arterial vessel should be oval/round and have an even, smooth surface.

Now that the arterial inflow has been examined in the transverse view, the evaluation of the longitudinal view should be completed—the access blood flow will be measured in this step. Although the access flow can be measured directly in the fistula or the graft, it is more accurate when measured in the inflow artery. The brachial artery should be used to measure flow in brachial artery fistulas as well as radial artery fistulas. This is because radial artery fistulas commonly get additional flow into from the ulnar artery via the palmar arch [3].

Pulsed-wave Doppler mode is used for flow measurement. To accurately measure the flow, the operator will need to accurately perform 3 steps: obtain an appropriate angle, proper vessel diameter measurement, and selection of cardiac cycles. It is important to establish the correct angle between the Doppler beam and blood flow direction (angle of insonation). The angle of insonation should be 60º or below, otherwise the measurement will be inaccurate with steeper angles overestimating flow. For a detailed review on the physics behind this see [5]. The angle of insonation is usually annotated on the right corner of the US screen.

To obtain an appropriate angle of insonation, the operator should adapt the position of the probe, select a portion of the vessel that has an advantageous angulation, or position and use the steer button to select a good doppler window. The next step should be to measure the diameter of the access. The final step is to select the span of cardiac cycles that the ultrasound will use to calculate the flow. One should obtain measurements over 2-5 cardiac cycles and report its average [6].

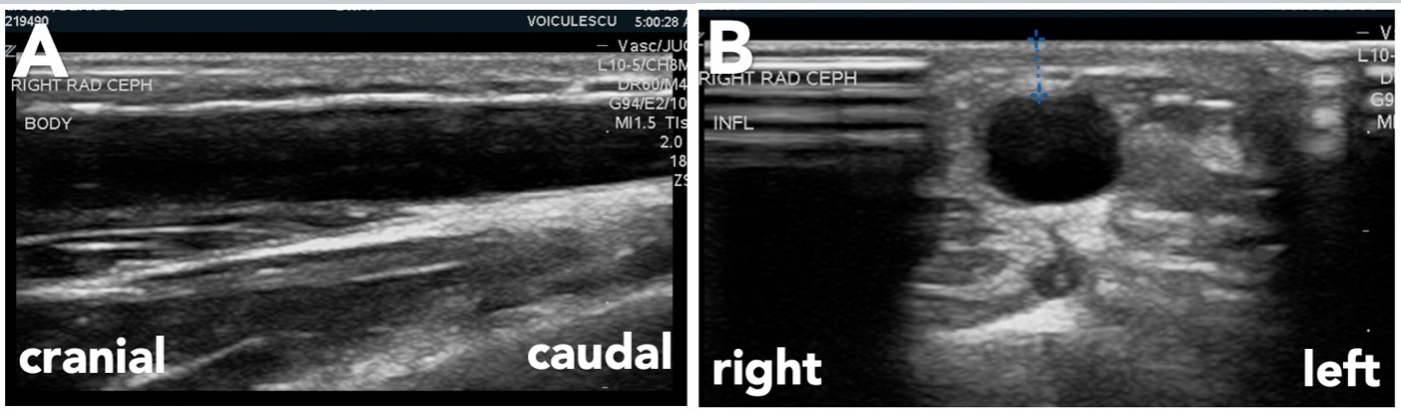

Figure 2. Ultrasound planes: A) longitudinal axis; B) transverse axis. Figures courtesy of Dr. Adina Voiculescu.

Now the venous outflow area should be examined. Just as with the arterial examination, positioning the transducer for a transverse view should be the first step. The operator should scan the vessel area looking for branching vessels or other changes. While the operator moves the probe, they should demarcate the access on the skin with a skin marker in order to "map" the access. After the first scanning through the region with a transverse view is completed, a longitudinal view should also be done in order to help with the mapping or confirm your findings.

In conjunction with physical exam, the access is now drawn on the skin. Size and depth of the access should be measured at several points along the course of the access. These measurements are made in B-mode in transverse axis. It is crucial to hold the probe as gently as possible and allow access to be visualized as a full circle. Pressure on the access from the probe can markedly affect the size measurement. Abnormal findings such as hematomas or pseudoaneurysms should be marked as well. See examples of mapped fistulas in Figure 3.

The best area for cannulation can be determined by the size and depth of the access. Ideally one would select a large superficial and straight segment with no overlying veins and optimally no nearby branching vessels. Generally, the access should be at least 5mm in diameter and less than 6mm deep in order to be optimally cannulated [7].

Maturation Assessment

In order to ensure that a vascular access is ready and is likely to deliver appropriate access to hemodialysis treatments, the physical exam should be coupled with POCUS assessment. 20%–60% of AVFs fail to mature for successful dialysis use [6]. POCUS does not replace the physical exam but enhances it. For example, while an access may meet the ultrasound criteria for maturation, it may not be clinically ready for cannulation and vice versa.

Maturation assessment is very similar to the mapping described above but takes into consideration the nuances of a new access. Post-surgical fluid collections such as seromas and hematomas are common and should be identified. Another consideration is that a new fistula often has branch veins which can affect maturation and these should be identified for safe cannulation and potential branch vein ligation.

There are three measurements that determine maturation by ultrasound criteria: blood flow, access depth, and access size. Different criteria or cut-offs for these measurements have been proposed and investigated.

Currently there are two adopted sets of ultrasound maturation criteria. The "rule of 6s" was first described in KDIGO guidelines in 2006 as an expert opinion and is still commonly used. It involves the following parameters: blood flow $\geq$ 600 mL/min, access depth $\leq$ 6 mm from the surface, and external diameter $\geq$ 6 mm [8]. The second set of parameters is the UAB criteria: blood flow > 500 mL/min and vein diameter > 0.4 cm. In a retrospective analysis of 69 patients who were 2-4 months post fistula creation, when both thresholds were exceeded, 95% (19 of 20) of the fistulas were adequate for dialysis. When neither threshold was achieved, only 33% (five of 15) of fistulas were adequate. Achieving just one of the two threshold values was associated with intermediate adequacy rates of 67%-70% [9]. Both KDOQI and UAB criteria were validated in the hemodialysis fistula maturation study (HFM) [10]. The HFM study was a large multicenter observational study, with over 600 patients which showed that AVF blood flow, diameter, and depth at 6 weeks post-surgery predicted AVF clinical maturation. The other factors that were considered included upper arm arterial diameter, presence of stenosis, presence of accessory veins, case-mix factors (age, sex, black race, AVF location, diabetes, dialysis status, and body mass index), and clinical center and did not further improve the AVF maturation prediction

Figure 3. Two examples of access mapping. The operator has drawn the direction and overall shape of the access and also measured its diameter (size) and depth at different location as well as average flow. In image A you can see the operator has identified a branching vessel. In image B the operator has signaled with arrows what they believe to be the optimal points for needle insertion.

[10]. As one might expect, the UAB criteria was more sensitive but less specific than the rule of 6s in predicting maturation.

The technique and steps to mark the fistula, identify branch veins and fluid collections, measure blood flow, and measure fistula depth and size are described above in mapping.

High Flow Fistula

Blood flow measurement be easily established via POCUS when a high flow access is suspected. Here POCUS is superior to physical exam alone because, while history might spark the diagnostic possibility, there are no specific physical exam findings and the direct measurement of access flow is required for a final diagnosis.

In patients with heart failure, pulmonary hypertension, vascular steal, or central venous stenosis, measurement of access flow is critical. Presence of high flow could be a major contributing factor and could be relatively easy to correct via banding or revision surgery. In absence of these conditions, it may be prudent to reduce flow in the fistula as a prophylactic measure to prevent long term adverse cardiac effects such as high output heart failure.

What is a high flow access is not well defined and is often relative to clinical picture. In patients with above listed conditions, any flow in excess to what is required for dialysis can be argued as high flow. In asymptomatic individuals, blood flow (Qa) of ≥ 2.0 L/min or Qa/Cardiac output ratio of >20% should prompt a discussion about prophylactic reduction in blood flow [11].

Vascular Steal

The diagnosis of vascular steal is predominantly clinical. The physical exam maneuver of compressing the access and then evaluating symptoms continues to be the recommended initial step to identify potential vascular steal. However, physical exam does not show the anatomical culprit of the issue. POCUS can be helpful in two ways: there might be signs of flow reversal when in doppler mode and, most importantly, vascular flow might be decreased.

Access Stenosis

Access stenosis can be assessed by POCUS via greyscale imaging in addition to pulsed-wave Doppler. The initial step is to use B-mode and search for presence of luminal narrowing. A narrowing of ≥50% of the access, when compared to the normal vasculature located upstream from the affected portion, is considered a positive finding. This can be done using the longitudinal or sagittal view. The second step is to determine if a peak systolic velocity (PSV) ratio between the anastomosis area of the access and the feeding artery 2 cm upstream from the anastomosis. This is done on longitudinal view. A PSV ratio >3:1 has been shown to be a very sensitive measure to suggest the presence of a stenosis. As discussed above, the measurement of flow and velocity in an access can be difficult, so if a PSV ratio is present but no stenosis is seen a fistulogram should be considered [4].

Hematomas, Seromas, and Abscesses

Infiltration during cannulation or due to movement of the needle during dialysis is common and can cause a hematoma. This can cause difficulty in cannulation of the access due to overlaying edema and fluid collection. In such a situation, use of POCUS in B-mode can localize areas of soft tissue swelling and fluid collection and identify sites that are safe for cannulation. The hematoma can also be measured and/or marked to allow for monitoring with future POCUS evaluation. Color Doppler can help identify active bleeding which should be promptly addressed.

In patients suspected to have access infection, B-mode POCUS should be performed to look for fluid collection. A fluid collection in this setting may be an abscess that needs to be drained.

In post-operative patients, fluid collection is commonly due to seroma. These are less inflammatory and appear less complex on ultrasound. POCUS in B-mode can identify and localize these collections and help with cannulation and monitoring.

Summary

Point-of-care ultrasound is an invaluable skill in the exam of dialysis vascular access. This inexpensive imaging modality can help guide proper cannulation and, in conjunction with the physical exam, establish access readiness and diagnosis of common issues. POCUS has been shown not only to improve patient's experience, but also decreases reliance on tunneled catheters and aids in accurate and timely diagnosis of many access related complications. Nephrologists and training programs should familiarize themselves with this technological tool so that we can continue to grow as a patient focused specialty.

Disclosures

None.

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